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JANUARY 1910

STORAGE

Volume III, No.

TRANSACTIONS

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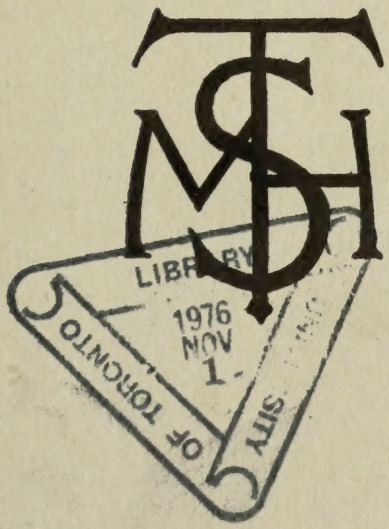
OF THE

SOCIETY OF TROPICAL MEDICINE AND HYGIENE



London:

SOCIETY OF TROPICAL MEDICINE AND HYGIENE

11 Chandos Street, Cavendish Square, W.

TRANSACTIONS

OF THE

SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

JANUARY, 1910.

VOLUME III. No. 3.

Proceedings of a Meeting of the Society, on Friday, December 16th, 1909,

DR. F. M. SANDWITH, *Vice-President*, in the Chair.

Death of Sir Alfred Jones.

Before the business of the meeting was proceeded with—

Sir PATRICK MANSON said he had a Resolution to submit to the Fellows of the Society. He presumed they were all aware that their distinguished President was not present that evening for a cause which was most unfortunately something in the nature of a calamity for

workers in Tropical Medicine. Professor Ross that afternoon had attended the funeral of Sir ALFRED JONES. Nobody acquainted with the history of the public recognition of the value of Tropical Medicine knew better than the Fellows present the important rôle that Sir ALFRED JONES had played in the furtherance of this subject, both in this country and abroad. When Mr. JOSEPH CHAMBERLAIN first brought to public notice the great importance of Tropical Medicine as a factor in colonial development, Sir ALFRED JONES, with characteristic energy and generosity, came forward with practical assistance. He was mainly instrumental in developing and supporting the School of Tropical Medicine in Liverpool, but his efforts were not confined to Liverpool. He looked upon the School of Tropical Medicine there as merely a means towards the end, viz., the fostering of Tropical Medicine in connection with the development of the Colonies; and as a consequence of this view he extended his interest to the London School also. He was a generous benefactor of the London School of Tropical Medicine, and indeed of any individual who showed a claim for consideration, whether as a leader or as a humble student in Tropical Medicine. He (Sir PATRICK MANSON) could speak personally for this. Although at first quite a stranger to Sir ALFRED JONES, in his (Sir PATRICK MANSON'S) visits to Liverpool and elsewhere, Sir ALFRED JONES had always extended a generous hand, and had always backed him up with his great influence. He (Sir P. MANSON) thought everyone interested in Tropical Medicine who came in contact with Sir ALFRED JONES, experienced the same treatment. It had therefore been suggested and it was his (Sir P. MANSON'S) privilege to warmly support the suggestion, that a resolution should be passed by the Society, and

forwarded to the family of Sir ALFRED JONES, to the following effect :—

> "That this Society, recognising the great services rendered by Sir ALFRED JONES, K.C.M.G., to Tropical Medicine, desires to record its appreciation of these services and sense of loss in his death. Further, that the Secretaries be instructed to communicate this Resolution to Sir ALFRED JONES'S family, and to convey to them the sympathy of the Society in their bereavement."

Sir HAVELOCK CHARLES said that when he saw the death of Sir ALFRED JONES reported a few days ago, he was forcibly struck with a sense of the irreparable loss which the School of Tropical Medicine at Liverpool had suffered. Sir ALFRED JONES had been a successful man in life; he was also a successful man in death, in that he had left behind him a reputation of doing good to his fellow men. It had been a great thing (as Sir PATRICK MANSON had just said) that, at a time when Tropical Medicine had but a few friends in England, a man with the determination and the good will of Sir ALFRED JONES had been present to give a helping hand. He desired to warmly second the resolution which had just been moved.

Dr. C. F. HARFORD, in supporting the motion, said he had had the privilege of knowing Sir ALFRED JONES for the past eighteen years, not only in connection with his work in furtherance of Tropical Medicine, but in what he had done for West Africa. He was confident that all the Fellows would recognise the splendid efforts he had put forward in the opening up of that hitherto very much neglected country, West Africa.

Dr. F. M. SANDWITH, who occupied the chair, said he was sure they would all emphatically agree with the

sentiments of the mover and supporters of the resolution. He would formally put to them the resolution which Sir PATRICK MANSON had read. He took it that it was their wish that a copy of that resolution should be sent to the family of Sir ALFRED JONES; but it had also been suggested that a similar resolution should be sent to the Liverpool School of Tropical Medicine, who had lost their head and chief ornament—their President; also that copies should be sent for publication in the *Times* and one of the Liverpool papers.

The resolution was thereupon put and carried unanimously.

MR. OTTO BEIT'S GIFT.

The following resolution, proposed by Col. OSWALD BAKER and seconded by Sir WILLIAM LEISHMAN, was then put to the meeting and carried unanimously:—

> "That the President be requested, on behalf of the Fellows of this Society, to convey to Mr. OTTO BEIT their high appreciation of the great benefit which he had conferred on the study of disease, including Tropical Disease, by his munificent grant for the endowment of research."

OBSERVATIONS ON THE MECHANISM OF INFECTION IN TICK FEVER,

AND ON THE

HEREDITARY TRANSMISSION OF SPIROCHÆTA DUTTONI IN THE TICK,

BY

LIEUT.-COL. SIR WILLIAM B. LEISHMAN,

Professor of Pathology, Royal Army Medical College.

GENTLEMEN,

Tick fever has, as you are aware, already furnished the subject for a discussion before the Society, a paper on it having been read by Dr. HARFORD[1] last year, while the morphology of the micro-organism which causes it, the *Spirochæta duttoni*, has also been discussed in a paper by DUTTON and TODD[2]. Under these circumstances I feel that some apology is needed for so soon re-introducing this disease as subject for discussion by the Fellows. Apologies are, however, tedious and uninteresting, so I shall only say that the branch of the subject with which I propose to deal is one in connection with which we still have much to learn, and has been the object of some investigations which I have been carrying out during the last two years, namely, the mechanism of infection and the hereditary transmission of the spirochæte through the tick.

Although I shall confine myself to this side of tick fever, the only one on which I can lay claim to first hand knowledge, I trust, however, that this may not have the effect of limiting the discussion, but that we may hear the views of those who are familiar with the epidemiological and clinical aspects, as well as those of such as

may be good enough to criticise the results of the experiments which I shall, without further preamble, lay before you.

For some years past I have been greatly interested in spirochætes, and have, among others, worked with *Pallida*, *Vincenti*, *Recurrentis* and *Duttoni*, both from the morphological and the biological sides, one of the principal objects of my investigations being the vexed question of their protozoal as against their bacterial nature. You are all aware of the opposing views which have been held on this point, and I must at once confess myself an advocate of the protozoal theory. I need hardly add that the solution of this point is of more than academic importance, and is intimately concerned with problems of immunity, and may possibly lead to successful prevention and treatment in the future.

The main facts in connection with infection in tick fever are well established, and I will only say that I have confirmed, if further confirmation were needed, the fact of transmission of the disease to animals by the bite of ticks sent to me from Africa. The hereditary transmission of the disease to the second generation of ticks I have also confirmed, as nymphs which I have reared in the Laboratory from the egg are infective for mice and monkeys. MOELLER'S[3] observation of the further transmission of the virus to the third generation I am not yet in a position to confirm, as my second generation has not yet attained sexual maturity.

Hereditary transmission through the tick, then, being established beyond doubt, my first observations were directed towards the discovery of spirochætes in the bodies of infected ticks, and long and carefully did I search those which I first received from Africa through the

kindness of my friend Capt. HALLAM HARDY, R.A.M.C., whose sad death from Sleeping Sickness you may have heard of. My search was in vain, no trace of a spirochæte was found. As these ticks had failed to infect a monkey by their bites I concluded that they themselves were not infected and asked for more, stipulating that, on this occasion, the ticks should, if possible, be collected from huts in which cases of tick fever had occurred. I need not trouble you with details of further failures, but I was in the end successful in infecting a monkey with tick fever by the bites of Ornithodorus, collected in Nyassa-land in infected huts. At the height of the fever, when the blood was rich in *Spirochæta duttoni* I allowed a large number of my ticks to feed on a monkey, and was then in possession of material with which to carry out the researches I had in contemplation,

I have already published a preliminary note in connection with these investigations in the Journal of the Royal Army Medical Corps[1], but it may be well to assume, as is probably the fact, that this has not come to the notice of the majority of the Fellows. I shall, therefore, endeavour to make as connected a story as is possible in the case of such a complicated problem without differentiating between observations which have already been recorded and others which have not yet been published. I hope before long to be able to put on record the details of the experiments themselves.

I mentioned just now that my first batches of ticks showed no spirochætes in any portion of their anatomy; to my surprise I was equally unsuccessful in my search in the case of the batch which infected the monkey, and, I may add, in the case of other batches since received from

different parts in Africa, which also proved infective. It is, of course, impossible to exclude the chance that some of the ticks which bit the monkeys in question did harbour spirochætes. This fallacy is one which is always present in such work as that under consideration. For example, whatever conclusion one arrives at as to the condition of a given batch or brood of ticks must be founded on the examination of a sample of such batch. However large the sample, and there are obvious limits to this where it is desired to follow up the course of subsequent events in such a batch, any conclusion is open to the objection that a different condition existed in a member of the group which was allowed to survive. Conservative surgery in the case of a tick is unfortunately impossible. The number of my examinations, however, totalling many hundreds, of ticks in all stages of development, enables me to say with a fair degree of certainty that no spirochætes were present in the tissues or body fluids.

Turning now to the hereditary transmission of infectivity to the second generation of ticks, which, as I have mentioned, I have personally confirmed, this confirmation was made with the progeny of ticks which, if infected, brought their infectivity with them from Africa and had only fed on normal blood since their arrival in England. Here again, no spirochætes could be found, either in the very youngest eggs which it was possible to dissect out of the ovary, in eggs at various stages of incubation or in the larvæ and nymphs hatched from such eggs. I may at this point remind you that the persistence of spirochætes in the tick, their presence in the ovaries and their presence in the eggs and in young hatched from these eggs, has been observed by Koch[5]

and, in part, confirmed by CARTER[6], the former working in German East Africa and the latter at the Liverpool School of Tropical Medicine. The negative results which I obtained were very puzzling in view of these positive ones, but I think now that they are reconcilable in the light of the subsequent experiments and observations which I shall mention.

I next turned my attention to a study of the fate of spirochætes ingested by ticks, dissecting a tick of each batch every day for a fortnight. In every instance the following were examined: the cœlomic fluid, the gut contents, the walls of the intestinal sac and portions of its diverticula, the genital organs, the salivary glands, the coxal glands, Gené's organ, the Malpighian tubes and Malpighian secretion. The result may be stated briefly, no recognisable spirochætes could be detected later than the tenth day. The changes which the spirochætes underwent in the intestinal sac were found to be very interesting, but would take too long to describe in detail. DUTTON and TODD[7] have described many of these changes, as well as others which were not encountered in my specimens. The principal features were the extrusion of lateral, more rarely terminal swellings, which contained one or more particles of chromatin, and the breaking up of the chromatin core of the spirochæte into numerous fragments of coccoid or bacillary shape. In a few instances these small chromatin particles have been observed free in great numbers in the gut contents. (*Fig.* 1.)

Long before this I had observed in the Malpighian tubules of almost every tick dissected aggregations of curious clumps of chromatin granules, often in such numbers as to mask the cellular structure of the tube. These granular clumps I subsequently encountered in all

stages of the tick's life from the microscopical ovum up to the adult. DUTTON and TODD have also noted granules in the Malpighian tubes of ticks recently fed on spirochæte blood, which they considered to be derived from the spirochætes, but I am in some doubt as to their identity with those in question, since Dr. TODD, to whom I had the pleasure of showing some of my specimens, informed me that he had not observed this condition in the tubes of young nymphs. I may say at once that I consider these chromatin granules to be derived from spirochætes, and, further, to be connected with them biogenetically. The situations in which they are encountered in the tick are, first, the Malpighian tubules, in which their distribution may be very irregular, some portions being distended by them (*Fig.* 2), while none may be found in a long tract of same tube. This irregular distribution may possibly be explained by the granules having escaped from the thin-walled intestinal sac into the tubules only in those situations in which the two structures happen to be in close contact. Second, in the ovary, where there are often encountered in great numbers and where, at times, a few clumps may be detected lying within the immature ova. Third, they are sometimes found in small numbers in the walls of the intestinal sac. Finally, as a very rare occurrence, similar clumps of granules have been seen in the cells of the salivary glands.

The shape, size and appearance of these granules may be gathered from the specimens which I have put under the microscope and by the micro-photographs (*Figs.* 1-6). From the time I first observed them, more than three years ago, I was suspicious of their possible protozoal nature, as they failed in many points to fit what appeared to me to be the only alternative explanations as to their nature,

DESCRIPTION OF PLATE.

The accompanying photo-micrographs were taken with Zeiss' apparatus fro films stained by Leishman's method.

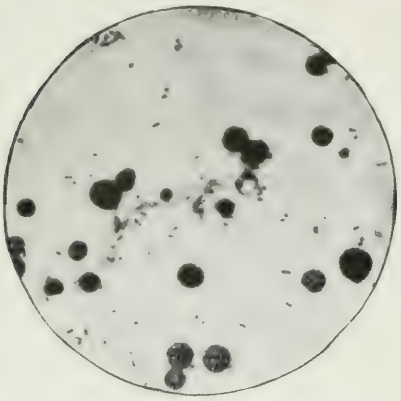


Figure 1.

Film made from the contents of the intestinal sac of a tick, two days after it had fed on heavily infected blood. The chromatin bodies are seen lying among the black granules of digested blood, also a few pale-staining spirochetes. Magnification, 1,000 diameters. (Page 81).

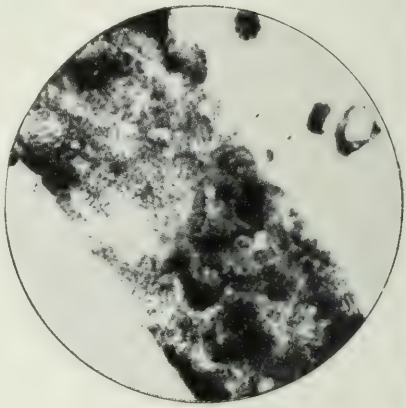


Figure 2.

Malpighian tubule of an infected tick, six days after feeding on infected blood, showing masses of the chromatin granules in the cells. Magnification, 1,000 diameters. (Page 82).

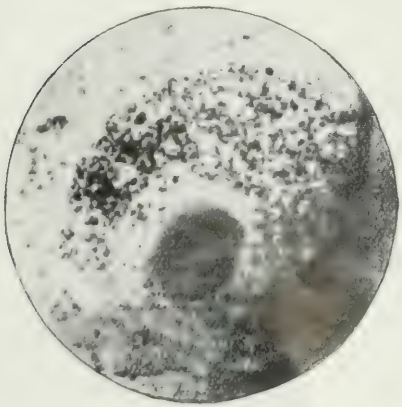


Figure 3.

Ovum projecting from the edge of the ovary, from a tick infected four weeks previously, showing many clumps of the chromatin granules within its substance. Magnification, 2,000 diameters. (Page 83).

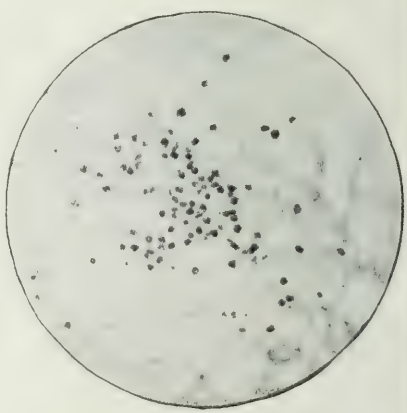


Figure 4

Clumps of granules in a film made from an egg just laid by an infected tick. Magnification, 1,000 diameters. (Page 83).

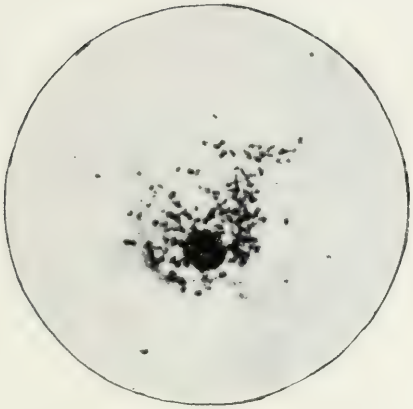


Figure 5.

Embryonal cell from an egg in a more advanced stage of development, showing numerous clumps of granules, many within the cell. Magnification, 1,000 diameters. (Page 83).

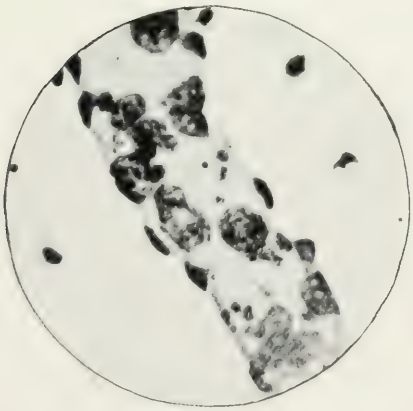


Figure 6.

Malpighian tubule of a young unfed nymph, showing a few masses of granules in the cells. Magnification, 1,000 diameters. (Page 84).

viz., 1st, artifacts resulting from the straining method employed; 2nd, granulations connected with the celular cytoplasm, and 3rd, bacteria. They appear to consist almost entirely of chromatin, although at times a faint blue-staining fragment has been seen attached to the granules or rods of chromatin. The tendency to adhere loosely in the form of little clumps is very marked, both in those granules which are stained in the un-ruptured tissues and in such as have been liberated by the laceration or division of such tissues.

During the prolonged search for spirochætes in the eggs, larvae and nymphs of infected ticks the same clumps of chromatin granules were almost invariably detected. From the youngest eggs recognisable under a high power in the teased out ovarian tissue, up to the young nymph hatched out from the egg they were observed at all stages. Only a small proportion, however, of the microscopic eggs showed granule clumps, and, as a rule, only one or two clumps were observed, with one exception, of which a photograph is shown, where a large number of clumps were seen, filling up the egg case (*Fig.* 3). In larger eggs which it was possible to dissect out from the ovary with fine needles the clumps were more abundant, while in mature eggs laid under natural conditions, they were rarely absent and often numerous (*Fig.* 4). The subsequent fate of these granules was studied from day to day after the eggs had been laid, and it was seen that, very soon after the first recognisable embryonal cells made their appearance, the granular clumps were found in the protoplasm of some of these cells (*Fig.* 5). At a still later stage, small masses of were seen, obviously in rapid growth, in which the cells clumps were once more found. From this point, all the granule clumps seen were intra-cellular, never free unless

the cells had been ruptured. Subsequent close investigation showed that such cell agregations were the primitive commencements of the Malpighian tubes of the young tick, every intermediate stage being seen up to such fully formed tubes as could be recognised without doubt, many of which, even at this early stage, showed the characteristic crystals of the Malpighian secretion in their lumen.

From this point up to the formation of the larva and the final emergence of the octopod nymph from the egg the granules were only to be encountered in the Malpighian tubules. (*Fig.* 6.)

Assuming their spirochæte origin it is obvious that these granules are not mere "resting forms" as they multiply in the egg and in the young tick, the few clumps seen in the most minute eggs giving rise to the thousands found at a later stage in the Malpighian tubes.

In all the subsequent stages of the growth of the nymph, at any rate up to the sixth moult, which is as far as I have followed the generation bred in the laboratory, they are constantly present in the tubules, though their numbers show great variations and the irregularity of their distribution in such tubules is sometimes very marked.

Contrasting nymphs hatched from females which had been known to feed on spirochæte blood with others hatched from females fed in the laboratory only on normal blood, there was no doubt that the granules were much more abundant in the case of the former; at the same time, the latter nymphs almost always showed the same granules, though in smaller numbers, though in a few instances I have been unable to detect any in the pieces of tube which were examined.

I may now proceed to describe some experiments aiming at the determination of the nature of these granules. Cultivation under very varying conditions gave nothing but negative results. Inoculations of mice, however, proved more successful. For this purpose various organs of ticks were carefully dissected out, washed in many changes of sterile salt solution, and finally broken up as far as possible by grinding in salt solution, the resulting emulsion being injected hypodermically into white mice. The presence or absence of spirochætes or granule clumps was noted by staining and prolonged microscopic search. In a certain number of cases positive results were obtained with emulsions of Malpighian tubules, of ovarian tissue, and of the white secretion of the Malpighian tubes; never, so far, with emulsions made from the salivary glands. The mice in these cases, after an incubation period of seven to ten days, corresponding with the uusal incubation period after natural infection by tick bite, developed tick fever and showed abundant spirochætes in their blood. In all cases in which infection occurred the granules were proved to have been plentiful in the tube or tissue inoculated, while no spirochætes could be found. As already mentioned, the failure to find spirochætes does not definitely prove their absence, but my search has been so close that I feel fairly confident that they were absent in the cases mentioned.

The positive results of the inoculation of emulsions containing such granules were not, however, obtained in all cases, and those which resulted in spirochæte infection were, in the majority of instances, derived from ticks which had been kept at a temperature of from 34° to 37° C. for a day or two before dissection. (Except where otherwise noted all the ticks were kept

at a temperature of 22° to 24° C.) Subsequent work leads me to think that the higher temperature has the effect of inducing changes in the granules which are an essential preliminary to their ultimate development into spirochæte form. This point will be mentioned again in discussing the effects of heat upon ticks recently infected with spirochæte blood.

A few words may now be said upon the method of natural infection by tick bite. It has, I think, been generally assumed, if not actually asserted, that this occurs by means of the injection of spirochætes through the biting parts of the tick, such spirochætes having previously harboured in the salivary glands. My persistent failure to find a single spirochæte in the salivary glands of a tick, even in such as had fed on heavily infected blood, appeared to me to throw some doubt upon the correctness of this view. At the same time, the inoculation of granules through the medium of the salivary secretion also appeared improbable in view of the extreme rarity with which I have encountered them in the salivary glands. An alternative method appeared to me as possible and was submitted to experimental test in the following way. Nine ticks, infected some months before, were allowed to bite a monkey; after they had fixed and commenced to feed they were gently removed and placed on another monkey on whom they were allowed to gorge. The fact of their all having bitten the first monkey was verified by observing the punctures and small ecchymoses which surrounded the bites. As is well known, when these ticks commence to swell they pass a large quantity of clear fluid from the coxal glands (whose anti-coagulating properties I have been able to determine) and some, in addition, pass the white

secretion of their Malpighian tubules. These fluids, therefore, bathe the skin of the monkey and almost certainly may penetrate into the subcutaneous tissues through the punctures left when the tick has loosened its hold on its host. The two monkeys, then, although bitten by the same ticks, differed in the following respect, on the first none of this fluid had been passed, while on the other the wounds were bathed in it. Some of the fluid passed on the second monkey was also collected and inoculated hypodermically into a mouse. Careful search of this fluid showed neither spirochætes nor granules, the latter, however, are so minute that they might readily be missed. The result of this experiment was interesting and suggestive ; the first monkey was not infected, while the second monkey, and also the mouse, developed tick fever which ran a typical course.

It would appear therefore from this experiment, and others of similar nature, that a possible method of infection, perhaps the common one, is through the medium of the secretions voided by the tick in the act of gorging and not, as usually supposed, by the direct inoculation of spirochætes in the veneno-salivary secretions.

This problem of the method of infection, however, appears to me to be still far from clear. Those who are familiar with the recorded experiments on tick transmission will recall that, in almost every instance, a number of ticks have been employed and not a single individual. I too have found that one cannot be certain of infecting an animal by the bite of a single tick, even when such tick is known to be one which is heavily infected. It is obvious therefore that other factors must come into play. One of these factors, though in my opinion by no means the only one, is undoubtedly the temperature at which

the ticks have been kept prior to their being allowed to feed. In Africa it has been shown that to secure the infection of animals it was necessary to bring the ticks down from the high and comparatively cool country and conduct the experiments in the warmer low ground. Again, most workers, before allowing ticks to feed, keep them for some hours, or for one or two days, at a temperature approximating blood heat, although the reason for this is usually held to be simply that it renders the ticks more active and more inclined to feed.

To my mind, this preliminary heating has a different significance, namely, that it has the effect of inducing certain changes in the granules which may be held as heralding their transformation into spirochæte form. It is hardly necessary to add that I do not make such a suggestion as a mere hypothesis, but as the result of many months' labour in the study of infected ticks kept under varying conditions of temperature. It would, however, occupy far too much time to describe these experiments in detail, and I shall confine myself to a brief summary of the results of the more important.

1. In nymphs of various ages and adults, which have been kept for a week or ten days at a temperature of 34° C., spirochætes have, in some instances, been seen to *re*-appear in various situations, chiefly in the Malpighian tubes and in the walls, not the lumen, of the intestinal sac and diverticula. These spirochætes, however, did not resemble *Sp. duttoni*, as encountered in the blood, they were shorter, more homogeneous and less regularly curved; they occurred, too, as far as could be observed, not free in the fluids, but actually in the cytoplasm of the cells lining the tubules and the intestinal diverticula.

2. The above change is preceded or accompanied by

an alteration in the character of the granules so constantly found in the Malpighian tubes; these become more coccoid or spherical in form, and many are enlarged beyond the usual limits of size.

3. Control material in the shape of ticks of the same batches, which had always been fed at the same time and on the same animal, but which had been kept at a temperature of 24° C., showed on dissection no trace of spirochætes, but only granules of the usual types and in the usual situations.

4. Spirochætes which have re-appeared in ticks under the above conditions of temperature, etc., may persist in such ticks for some months after they have been replaced at the lower temperature, and are found in the same situations, though in smaller numbers.

5. Young nymphs newly hatched from infected parents, when kept at a high temperature, show the same changes in the character of the granules as older ticks and adults, but spirochætes have never been noticed. This would suggest that a feed of blood may be another factor in inducing the change into spirochæte form.

6. A comparative study has been made of newly hatched nymphs whose first meal consisted of spirochæte blood, and which, were subsequently divided into three lots and kept at three different temperatures. For this purpose nymphs of each group were examined daily up to three or four weeks after feeding.

(*a*). In nymphs kept at the lower temperature of 24° C. the ingested spirochætes were found to undergo speedy segmentation of the chromatin and, after a period of ten to twelve days, were found to have disappeared completely from the stomach: later than this, no spirochætes could be detected in

any situation in the nymph's body. An increase in the number of granules in the Malpighian tubes appeared to coincide with the disappearance of the spirochætes from the gut, but this point was difficult to verify in view of the constant presence of the granules in almost all ticks and the variable numbers encountered in different individuals.

(*b*). Nymphs kept at a temperature of 34° C., showed similar changes in the ingested spirochætes, but such changes and the disappearance of the spirochætes from the gut occurred more rapidly than in those kept at 24° C. A few days after the spirochætes had disappeared, they *re*-appeared in the tissues and fluids of the nymph, but in greatly altered form, most being very much shorter than any of those usually seen in the blood, and some little larger than cholera vibrios. While the smallest forms of *duttoni* as seen in the blood are about 16μ to 19μ in length—DUTTON and TODD[8] mention one of 13μ—many of these "young" forms, as I may call them, are no more than 8μ to 9μ. These young spirochætes persisted as long as the ticks were kept at this temperature, but rapidly disappeared when they were replaced at 24° C. In some situations it was apparently possible to trace the origin of the young spirochætes out of the granules. (Sketches of these developing forms are shown.)

(*c*). Nymphs kept at a temperature of 37° C. showed a similar condition as regards the spirochætes to those kept at 34° C.; the young spirochætes appearing after the ingested ones had disappeared from the gut, but in this case they were not so abundant, doubtless on account of the impaired

vitality of the ticks which, at this temperature, will not moult, and eventually die in about three or four weeks.

7. Attempts made with a view to the detection of spirochætes in the eggs laid by infected parents. Out of many hundred eggs examined, it is only recently that spirochætes have been encountered, and this in four eggs only. Two of these were eggs laid by a tick which had been heated for five days at 37° C. some months before, but which had subsequently been kept at 24° C. In this case the spirochætes were scanty and of the usual adult form. The two remaining eggs were dissected out of the ovary of a tick which, after feeding on normal blood, had been placed at 34° C., and kept at this temperature for nearly four weeks before dissection. In this instance the spirochætes were extraordinarily abundant; they occurred in great tangles, and many of them appeared to be in process of development out of the granules. Sketches of some of these forms are shown, and the original specimen is displayed under the microscope.

With regard to the influence of previous heating of the ticks as bearing upon some of the experiments to which I have alluded. It is of course possible, in cases in which infection of the animal resulted, whether through the agency of the bite of a tick or through the inoculation of tissues or secretions that spirochætes may have been present although they escaped observation. It does not appear practicable to exclude this possibility. At the same time, the most arduous and prolonged research of the material inoculated, or of the tissues of these ticks dissected after they had fed, has in many instances resulted only in the demonstration of the granules. In some cases in which infection was successful, the

ticks employed had been heated for from one to four days at 37° C. As just mentioned, prolonged heating at this temperature has, in some instances, resulted in the re-appearance of what I have called young spirochætes. The question arises, therefore, whether infection in these cases may have been due to the inoculation of such young spirochætes, and not, as I have suggested, to the inoculation of the granules. I do not feel able at the present moment to speak with confidence on this point, and will only say that the general analysis of my results leaves me with the impression that inoculation of the granules alone *will* cause infection, but that it appears probable that previous heating of the tick is an essential preliminary, inasmuch as it induces changes in the granules which are the initial stage of their conversion once more into spirochætes. I may add, in connection with this question, that a considerable number of mice inoculated with material containing granules only, although not becoming infected, died in 24 to 48 hours, although but a small dose was inoculated, and this subcutaneously. A bacterial septicæmia was excluded in these cases by the post-mortem examination.

Two further observations made in the course of these investigations appear worthy of record before I proceed to my concluding remarks.

First, the development of immunity in the case of the monkey. One of the monkeys infected by tick bite recovered, an exceptional experience, after the third relapse. Infected ticks were allowed to feed on this monkey four weeks after recovery, and infection again resulted; but in this instance there was no relapse. Five months later, the bites of another batch of infected ticks resulted in the appearance of very rare spirochætes on the

eighth and twelfth days only, while a fourth feeding, one month later, demonstrated at last an apparently substantial immunity since no spirochætes were subsequently found.

Second. On two occasions I have observed clumps of the granules in spermatozoa found in the oviduct of an infected female. It appeared to me in these cases that there was no doubt as to the actual inclusion of the granules in the spermatozoon, as opposed to possible super-position. If this was the case, and if my views as to the nature of these granules prove correct, this suggests an interesting possibility as to the method by which the young intra-ovarian egg becomes infected, while it would not be unreasonable, on grounds of analogy, to suspect that a similar procedure might occur in the case of the hereditary transmission of the Treponema pallidum.

I shall resist the temptation to theorise upon the manner in which this view of the life history of *Spirochæta duttoni* fits in with the facts known as regards other spirochæte infections, and will only point out that such a cycle of development would, in my opinion, afford a more satisfactory explanation of the mechanism of the relapse than some of the others which have been put forward.

In conclusion, gentlemen, you will realise that experiments such as I have described are, inevitably, long drawn out, and, from their nature, exceptionally difficult of interpretation. It is also inevitable that the necessary confirmation, if such be forthcoming, cannot be rapid. I may mention, however, the few pieces of confirmatory evidence which have come to my knowledge since the publication of my preliminary note. First, Professor NUTTALL was good enough to confirm my observations as to the presence of these granules in the eggs and ticks

which I sent to him, and also to inform me that he had failed to find them in similar situations in some other Argassine ticks.

I may add in this connection, that I have recently had the opportunity, through the kindness of Dr. GRAHAM SMITH, of examining some *Ornithodorus savignii*, which he had obtained from the neighbourhood of Khartoum. These ticks are so closely allied to *Ornithodorus moubata*, that the microscope is needed to differentiate them, and their internal anatomy appears to me to be essentially the same. A careful search of the Malpighian tubules of the five ticks which I have dissected has shown no trace of any of the granules which I have mentioned as being almost invariably encountered in this situation in *Ornithodorus moubata*. This negative evidence appears to me to have a certain confirmatory value.

Although not directly connected with the present subject, I should like to add that I found in the Malpighian tubules of these *Savignii*, enormous masses of what appeared to be a bacillus, growing in long segmented threads, recalling a pure culture of Anthrax bacilli, but on a much smaller scale. They were present in every tick, and the appearance was so striking and unusual, that I find it hard to resist the impression that they represent the virus of some disease which this species of tick may transmit. At all events, they are sufficiently remarkable to put on record, and I have placed under a microscope one of the specimens which shows the organisms in a portion of a Malpighian tube. It would be curious if further experience should prove this to be an instance of the demonstration of the cause of a disease before the disease itself has been investigated.

Second, Dr. BALFOUR[9] on searching the *Argas*

persicus which transmits the extremely interesting fowl spirochætosis of the Soudan described by him, encountered similar granules in infected ticks, and was also able to confirm some of my experiments by injecting emulsions of tissues containing these granules, but no spirochætes, with the result that the chick injected contracted spirochætosis.

Third, I have recently been informed by Dr. DARLING that he has found granular forms in the tissues of animals infected with the spirochæte of the relapsing fever occuring in the Isthmus of Panama, which granules he also suspects to be biogenetically connected with the spirochætes and that inoculation of such tissue, apparently completely free from spirochætes, was followed by infection.

These observations are naturally encouraging, but I should like it clearly to be understood that no one realises better than myself how far some of my results are removed from absolute proof and how much they stand in need of control and confirmation.

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Sir PATRICK MANSON, in opening the discussion, said that, in common with everyone present, he recognised the extreme importance of Sir WILLIAM LEISHMAN'S paper, for if the hypothesis he had expressed proved to be well founded, it probably had in it the solution of the problem of the method of infection by the tick, not only in the case of spirochætes, but of other and similar diseases of perhaps equal, if not more, importance. Sir WILLIAM LEISHMAN had brought out three or four facts of extreme interest. Certain inferences which he had suggested were perhaps not proved up to the hilt, but he had given them facts of importance; for example, the influence of temperature in forwarding the development of spirochætes to the infective stage in the tick. There were diseases which had their seasonal epidemic manifestations; the seasonal epidemic character of these diseases might depend upon a similar influence of temperature on the germ in the course of its transmission—scarlet fever, for example. The only criticism which he (Sir PATRICK MANSON) could make—and, indeed, Sir WILLIAM LEISHMAN had made the criticism himself—was the absence of control experiments at certain stages of the investigations, and he could not help feeling a certain suspicion that it might be that the granular bodies Sir WILLIAM LEISHMAN had found in the Malpighian tubes were not connected with spirochætes at all. Everyone who had had much to do with microscopical investigation of the contents of the intestinal canal and connected organs of athropods, knew full well what a splendid field these organs afford for microscopic life. In examining the Malpighian tubes of mosquitos he (Sir PATRICK MANSON) had many times found them filled with protozoa of various kinds; and he had seen over

and over again larval forms of different organisms whose nature he could not pretend to recognise. The thought suggested itself that possibly the granular material or bodies which Sir WILLIAM LEISHMAN had described might be, so to speak, accidental and unconnected with the spirochæte. He (Sir PATRICK MANSON) could have wished that Sir WILLIAM LEISHMAN had been able to give them more details of the controls he had used in his investigations, and to have told them how often he had examined the Malpighian tubes of ticks which had been fed on non-infected individuals, and why, if he had seen these granular bodies in non-infective ticks, these ticks had failed to convey the disease. These were questions which he (Sir PATRICK MANSON) was quite sure Sir WILLIAM LEISHMAN would be the last to resent, and which, perhaps, he would be able to clear up in future communications.

Dr. G. C. LOW said that the principal question which suggested itself to him was of the same nature, viz., as to what controls had been carried out on apparently non-infected ticks. The observation on the ticks that sucked the normal blood of a monkey was interesting, but there was the possibility that Sir WILLIAM LEISHMAN'S ticks might have been infected, and it could not be said even that the original African ticks did not have infection. It was absolutely certain that the parasite did go through the tick because of its progeny being infected, and (especially after BALFOUR'S work on the fact of the spirochætes going into corpuscular blood) it was also evident that the spirochætes did not go through the tick as spirochætes: because if they did so, of course Sir WILLIAM LEISHMAN would have seen them. They,

therefore, must go through the tick in some changed form, and if this were so he thought it exceedingly likely that the granules observed by Sir WILLIAM LEISHMAN were forms of spirochætes. The prophylaxis of the disease appeared to be simple, because if one avoided sleeping in native houses and always pitched one's own tent, there was absolutely no chance of becoming infected. If one slept on the floors of the native houses there was a great chance of getting the disease, because practically all the ticks in the houses were infected. In the time of LIVINGSTONE the disease, as he described it, was evidently very deadly, but nowadays it did not appear to be specially so. The proportion of deaths was small. It did not seem to be as deadly as ordinary relapsing fever seen in Europe and other places.

Dr. BAGSHAWE said that he was interested in the monkey, and he would like to ask Sir WILLIAM LEISHMAN if he could tell the Fellows how long immunity lasted; whether it disappeared soon or whether it lasted a long time.

He had recently come across some notes relating to tick fever, one of which had bearing on the infectivity of the fluid which bathed the wound. Two observers in Germany (SCHUBERG and KUHN) experimented with *Stomoxys calcitrans* in order to find out whether *percutaneous* transmission of spirochætes was possible from the squashing of flies which had gorged on a sick animal. They squashed five flies which had been infected with Russian relapsing fever, and succeeded in infecting in that way healthy white mice. They merely squashed the flies on the skin, and they found that the mice, five or six days after, had spirochætes in their blood. That was remarkable, and from this it would

appear that if infected blood was in contact with the skin under certain conditions it was not necessary that there should be a puncture wound. These same observers also carried out feeding experiments with *Stomoxys*. They tried to convey the disease by interrupting the *Stomoxys* in the act of sucking a sick animal and putting it upon a healthy animal, and reported that they succeeded.*

As to the treatment, he believed up to the present there had been very little success in the treatment of relapsing fever. Dr. HATA (a pupil of Kitasato) had been trying two substances at Frankfurt (reduction stages of disubstituted phenyl-arsenic acid, and had found them strong spirillicides. HATA had treated mice which were infected with the spirochætes of relapsing fever, and found that to cure them he had only to use one-third of the maximum dose which the mice would tolerate. One and a half milligrams per kilo of one of these compounds was sufficient to cure an infected fowl, and that appeared to be a dose which, if applied to man, would amount only to one-tenth of a gram.†

Dr. L. W. SAMBON said he was very greatly impressed by the thoroughness of Sir WILLIAM LEISHMAN'S investigations and experiments. He thought he had seldom heard of experiments carried out in such a masterly way. He did not think anyone who had once seen these peculiar "chromatin granules" would experience much difficulty in recognising them, whether they were in ticks

* Deutsche Militärärztliche Zeitschrift, 1909. Heft 23. See also Nattan-Larrier. Bulletin de la Société de Pathologie Exotique. 1909. Mai, No. 5, p. 239.

† Zeitschrift fur ärztliche Fortbildung, 1909. 1 Dezember. p. 721.

or in anything else. They were only found in infected ticks, and he thought Sir WILLIAM had told them that in certain ticks of another species he had not seen these granules. His (Dr. SAMBON'S) work on this group of hæmoprotozoa had unfortunately been very limited. However, in 1907, he had had the opportunity of examining similar bodies found by Dr. BALFOUR within the erythrocytes of Sudanese fowls, and he had suggested that they probably represented a peculiar stage in the life-history of the spirochætes of fowls. He used the word "spirochæte" because others had used it, but, in 1906, he had suggested another name, viz., Spiroschaudinnia, which had already been adopted by Professors LUHE, WARD, and others. After what Sir WILLIAM LEISHMAN had told them of the life history of these protozoal parasites, he thought it was high time that a new name should be used to indicate these forms. The name "spirochæte" had been given by EHRENBERG to a free living form, the bionomics of which were very different from those of the parasitic forms inhabiting the blood of vertebrates. He thought, therefore, there was very good reason for classing these parasitic forms into a separate group to be called spiroschaudinnia.

Captain R. G. ARCHIBALD, R.A.M.C., said that during the past summer he had been working with Ornithodorus Moubata and Ornithodorus Savignyi, and had conducted numerous dissections of the internal organs of these ticks, but had not succeeded in finding the "granules" which Sir WM. LEISHMAN had described in his paper. The O. Savignyi had been collected from the vicinity of a well near Khartoum, and the O. Moubata had been sent to him from Uganda. Feeding experiments with

these ticks had failed to produce Spirochætosis in susceptible animals. He mentioned these facts, as the ticks evidently appeared to be non-infected ones and possibly afforded controls to the experiments of Sir Wm. Leishman.

Mr. T. P. Beddoes said that the laboratory experiments tend to confirm the hypothesis that infection of the human embryo with syphilis occurs only in the maternal economy. He hoped that further investigation would establish the analogy between the granules in the spermatazoon in the oviduct of the tick with a yet undiscovered phase of Treponema pallidum in the human embryo in the uterus. These experiments might establish the view that every mother of an infected child is herself infected and requires immediate and prolonged treatment; otherwise in his opinion, tertiary symptoms would be almost certain to occur, and future children would be liable to inherit infection.

Dr. Yale Massey said that with regard to Sir William Leishman's description of transmission of the organisms under the influence of increased temperature, he called to mind that quite a large number of natives who had been transferred from the Kabinda district, in the Congo, which has an altitude of about 2,000 feet, to the Katanga district at an altitude of 5,000 feet, developed the disease. Those natives were perfectly familiar with Ornithodorus Moubata in their own country and Dutton and Todd had found tick fever prevalent in the same district. It appeared that at the district in question, which was about 400 miles distant and at a much higher altitude (about 5,000 feet), a large number of those

natives developed spirochætes and there were several deaths. The difference in the climate, the higher altitude being much colder, seemed to affect and lower their vitality to a very great extent. They did not seem very strong and a great many died; some were also infected with sleeping sickness. But it was the influence of vitality in the matter of virulence which had struck him in these cases. The natives seemed, as he had said, to be quite familiar with the disease, and probably were immune so far as their native place was concerned, but put in a climate were the vitality was lowered, they seemed to develop the disease.

He might say as regards the statement as to the ease with which relapsing fever could be avoided, that he could not agree that it was easy. It was difficult to keep Ornithodorus Moubata out of the huts, especially in the part of the country where the houses had thatched roofs. In fact, it was quite impossible to get rid of the parasites without burning the buildings, and consequently one might really run a great risk of contracting the disease.

Dr. C. M. Wenyon thought it probable that some relation existed between the granules just described by Sir W. Leishman and the somewhat similar granules described by Balfour in the red blood corpsucles of Khartoum chickens. It was perhaps known to the majority of the Fellows that Balfour in Khartoum had found that chickens suffer from a spirochætosis as they do elsewhere, These chickens may recover from the spirochæte infection, or they may enter upon what is described as an after phase of the disease in which spirochætes are absent from the blood, but peculiar

granules appear in the red blood corpuscles. BALFOUR thought that these granules are produced from spirochætes which had penetrated the red blood corpsucles. It occurred to him (Dr. WENYON) that it might be of interest to produce this after phase in chickens at home. Dr. BALFOUR had very kindly supplied him with infected Argus Persicus from Khartoum. With these ticks he infected chickens at the London School of Tropical Medicine. In the case of very young chicks two or three days old the infection was severe, and proved fatal. With older chicks and adult hens the disease was mild, a complete recovery being the usual result. The point of interest, however, was that in no case was there an after phase like that described by BALFOUR in the Khartoum chickens, and further, the peculiar intracorpuscular granules so characteristic of this after phase did not appear. It was of course possible that the difference in climatic conditions of the two places accounted for the variation in the course of the disease. As regards the questiou of immunity, he stated that he had been able to infect one hen on three separate occasions at intervals of about two months. He would very much like to know what were the views of Sir W. LEISHMAN on the relation, if any, existing between the granules which he had described from Ornithodorus, and the granules of BALFOUR from the Khartoum chickens.

Dr. F. M. SANDWITH stated that he had recently had the opportunity on two occasions of visiting Sir WILLIAM LEISHMAN, at the Royal Army Medical College, and seeing some of the ticks of which so much had been said. He was quite sure that he would be expressing the views of the Fellows when he thanked Sir WILLIAM LEISHMAN,

on behalf of the Society, for the trouble he had taken in preparing the valuable and interesting paper which he had contributed, which had given great pleasure to those who had listened to it.

Sir WILLIAM LEISHMAN, in replying to the various points which had been raised, said that Sir PATRICK MANSON and Dr. LOW had both commented, with perfect justification, on the absence of controls. Such controls, in the shape of un-infected ticks, were just what he had been searching for in vain. When a tick was infected, infection passed to the second and third generation, where then was it going to stop? From the constant presence of the granules, he was inclined to believe that almost every tick was infected, though not necessarily infective. He had spoken of ticks at the beginning of his paper as not infecting a monkey, Such ticks had not been heated but he found in all of them the same granules. If he had heated the ticks possibly they would have proved infective, Batches which he now had, became by heating almost always infective. If one could only get a batch of ticks which were definitely known to be uninfected that, of course, would settle the question one way or the other. Sir PATRICK MANSON had also referred to the variety of micro-organisms of all sorts which he had found in the Malphigian tubes of mosquitos. As regards Ornithodorus Moubata, in all the Malpighian tubes which he (Sir WILLIAM LEISHMAN) had examined he had never seen a single bacillus nor a recognisable protozoon. The only thing he had seen were those curious chromatin granules. Dr. LOW had made the comment that, even supposing the theory as to these granules were correct, it was not a matter of great importance. He (Sir WILLIAM LEISHMAN)

could only say that he did not agree with Dr. Low, because, apart from the question of tick fever, if one were able to prove that this blood spirochæte was a protozoon and went through a cycle of development, he thought that the bearing of such an observation upon the life history of other spirochætes, notably that of syphilis, might prove of very great importance indeed. Dr. Low had also stated that the disease was easily avoided; a subsequent speaker, however, had spoken otherwise, and had, indeed, voiced his (Sir WILLIAM LEISHMAN'S) views on that point. Dr. BAGSHAWE had asked him how long the monkey whose case he (Sir WILLIAM LEISHMAN) had had quoted remained immune. The last observation was made about two months ago, and infection had not since been attempted. Dr. SAMBON had made a proposal for a change of name from Spirochæte to Spiroschaudinnia. Dr. SAMBON had his (Sir WILLIAM LEISHMAN'S) sympathy in the suggestion, as there was undoubted confusion in the present terminology. Lieutenant ARCHIBALD had mentioned that in some Ornithodorus Moubata procured in Uganda, he had failed to find these granules, and, also, that he had failed to infect his animals by allowing such ticks to bite them. Possibly those were the controls which he (Sir WILLIAM LEISHMAN) had been searching for; perhaps, also, the other factors mentioned on the paper were brought into play and accounted for the failure of infection. In reply to another Fellow who had been interested in the finding of granules in spermatozoa, he might add that he had examined very closely spermatozoa in the genital organs of male ticks, and he had found that although the males harboured granules, just the same as the females, none were to be seen inside the spermatozoa in the case of the

male tick. Finally, he had been asked his opinion as to the granules found in the fowl's corpuscles in Dr. BALFOUR'S investigations. He had studied these with great interest and had come to the same conclusion as he believed Dr. BALFOUR had done, namely, that they were part of the life cycle of the spirochætes, and he thought that these granules probably indicated a somewhat similar cycle of development to that which he presumed occurred in the case of Spirochæta Duttoni.

TWO CASES OF NON-ULCERATING "ORIENTAL SORE," BETTER TERMED LEISHMAN NODULES.

BY

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INTRODUCTORY.

There came recently, under the care of one of us (D.B.T.), an Egyptian soldier (Case I.) with a peculiar skin lesion, the character of which is well shown in the accompanying photographs taken by Dr. BEAM. The patient was sent to the Wellcome Research Laboratories, where it was suggested that it would be well to examine the contents of the skin lesions and also to make a histological examination of the growths. This was done by one of us (A.B.) with the result that large numbers of a species of Leishman-Donovan body, presumably *L. tropica*, were found, but while some sections of the growths bore a close resemblance in their pathological histology to true oriental sore, others presented peculiar features. Indeed both clinically and histologically the condition was at first suggestive of that rare skin disorder which bears many different names, but is perhaps best described as benign multiple cystic epithelioma or epithelial cystadenoma of the skin. The history showed that we were dealing with a disease of considerable

interest, an interest not lessened by the discovery of a second very similar case, which in all probability had become infected from the first.

It is proposed in the present paper to discuss the condition generally, to give the clinical histories of the two cases, and to deal with the microscopic findings, leaving till a later period the account of the attempts which are being made to cultivate the parasite, the animal inoculations, the feeding experiments with insects and the question of prophylaxis and treatment.

Case I.—Ahmed Hussein (*Fig. 1*), soldier in No. 4 Company, 16th Battalion, Egyptian Army; age 20, an Egyptian fellah from the village of Nezli Bedeni in the Mudirieh of Minieh, Upper Egypt. He is a stoutly built man, not very intelligent, in good condition, but not of such fine physique as is usually seen amongst the Egyptian soldiery. He has had five months' service in the Egyptian Army, the last four months of which have been spent in the Sudan.

Admitted to the Military Hospital, Khartoum, on October 9th, with soft, pink, keloid-like raised growths on the face, neck, shoulders, arms, back and inner surface of the thigh.

Family History.—Father, aged about 70, developed *similar growths six years ago*, and at the present time they are more numerous and much larger on his body than on that of his son. Since the growths appeared he has become a lunatic and has lost his hearing. The tumours are said to be in some instances many inches in diameter, and *have never showed any sign of ulceration or breaking down.*

Mother dead, cause unknown.

Brothers: One brother and one step-brother. Neither

Figure 1.

CASE 1.—Growths on face, neck and left arm. (Page 108).

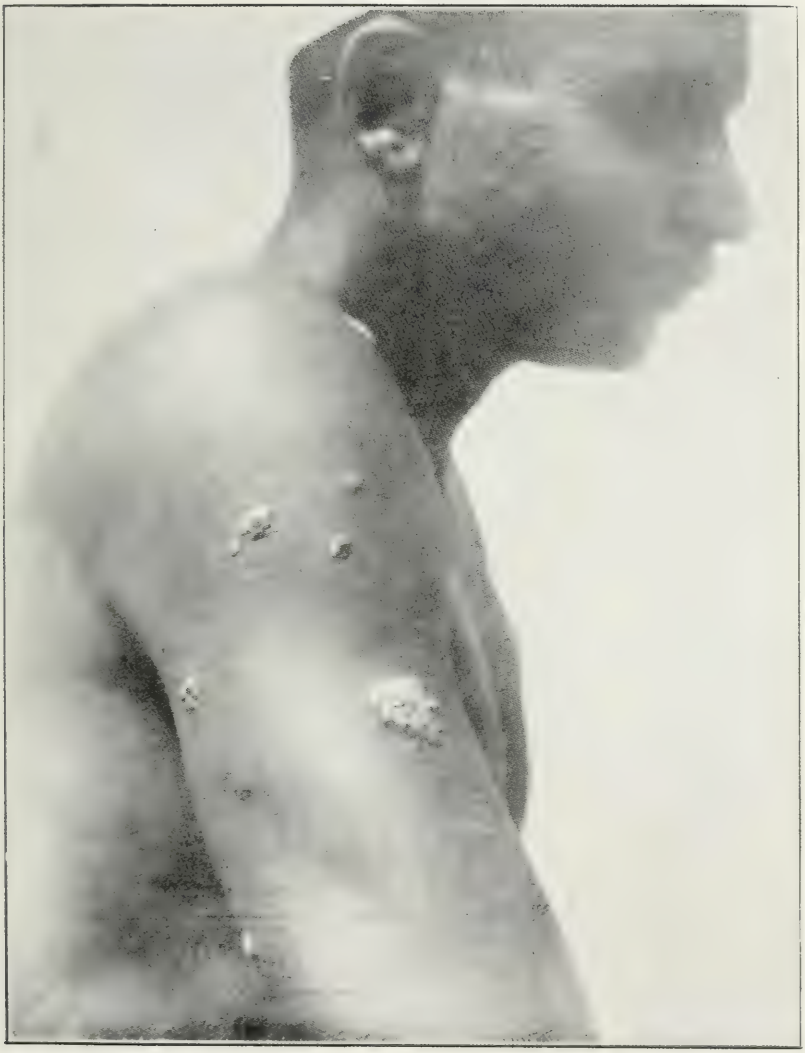

Figure 2.

CASE I.—Growth on right shoulder and upper arm. Those showing scabs have been punctured. (Page 109).

are affected. The former, aged about 40, would appear to be phthisical.

Sisters: Six in number and all unaffected save one. Eldest aged about 35. Youngest about 12 years. The eldest sister is married and has three girls, all healthy. The second sister has two children, a boy and a girl, both healthy, the third sister has one girl who is healthy, *but the mother has for the past four and a half years suffered from the same skin disease as her brother.* She became infected when living at home, and in her case the tumours are about as numerous as in the brother's. Her husband shows no sign of the disease.

The fourth sister has one girl, who is healthy. The two youngest sisters are unmarried.

A paternal uncle died of phthisis four years ago. An aunt, aged 75, is healthy. Patient's grand-parents are dead, cause of death unknown.

Personal History.—As a child patient had small-pox. There is no history of any venereal complaint. No history could be obtained as regards the presence of insect parasites in his house or village.

History of present illness.—The growths, which, as will be seen, occur for the most part in groups (*Fig. 2*), began to appear first of all upon the left side of the neck, two years ago, when he was living in his native village. Then the left side of the face became infected eight months ago, followed by the right shoulder and right upper arm six months ago. Four months ago the neoplasms appeared on the outer surface of the left forearm, and fourteen days ago very small papules presented themselves on the inner surface of the left thigh, about the region of Scarpa's triangle.

In addition, growths, the date of appearance of which

is uncertain, are present over the insertion of the left deltoid, and nearly in the centre of the back slightly to the left of the spinal column.

The growths are said by the patient to appear first as small pink circular points raised above the surface of the skin and of about the size of a pin's head. They grow until they reach the size of a pea, when secondary points appear to develop at the periphery of the primary growths, and as a rule separated from these latter by narrow tracts of healthy skin. These secondary tumours develop and become absorbed into the parent growths. As a result the main tumours increase in size and the whole mass takes on an irregular shape.

The patient complains that the growths itch intensely when exposed to the sun's rays, and that they pain him when pressed or when they come violently into contact with anything hard.

The people of his village pronounced him "Waash," *i.e.* unclean, and refused to eat with him.

Clinical Examination.—General appearance healthy, expression dull and apathetic, no wasting, no sign of any systemic disease, no glandular enlargement. Heart, lungs, liver and spleen normal. Urine: no sugar, no albumen.

The growths in the situations indicated resemble nothing so much as the mountains on a relief map (*Fig. 3*) looked on from above. There is the main elevation with spurs and ridges projecting from it, these latter representing the secondary growths which have united with the parent lesions. The tumours are of a definite pink colour, contrasting well with the brown pigmented skin, have a shiny aspect, are neither scaly nor ulcerated, and show no signs of breaking down. To the touch they feel smooth, firm, yet soft in consistency, are easily moveable and are not adherent to the deeper tissues (*Fig. 4*).

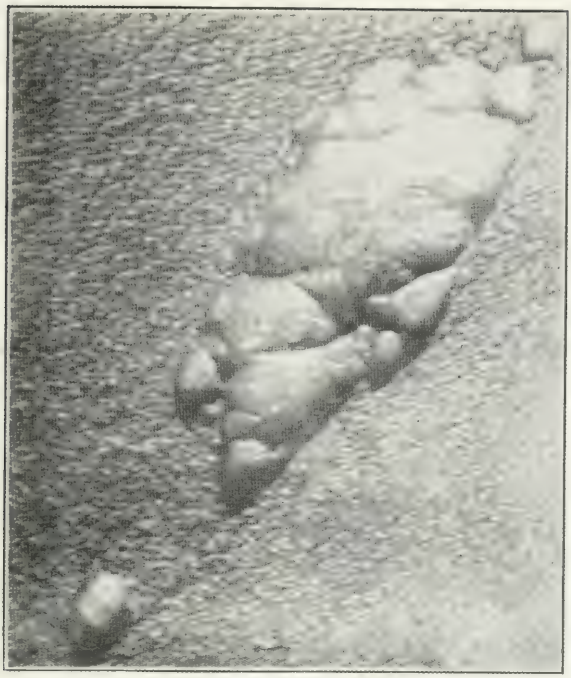

Figure 3.

CASE I. Neck growth. Twice natural size. (Page 110)

Figure 4.

CASE I. Neck growth. Page 110.

When punctured they either yield blood alone, or blood with serum, or blood and a small quantity of white cheesy sebaceous-like material. After puncture the site of injury heals readily, and a small scale or scab forms. This is well seen in *Fig. 1.* On section to the naked eye the growths appear fibrous. The following are the measurements of the growths :—

On the face ...	20 mm. by 18 mm.
On the neck ...	35 mm. by 15 mm. (*Figs. 3 & 4.*)
Over insertion of left deltoid ...	5 mm. by 5 mm.
On outer surface left forearm ...	not measured—excised.
On right shoulder...	20 mm. by 14 mm.
On right upper arm	29 mm. by 18 mm.
On left thigh ...	2½ mm. by 2½ mm.
On back	2½ mm. by 2½ mm.

Blood examination.—An examination of blood taken from the finger made on October 10th, showed 6,050,000 red blood-corpuscles and 5,600 leucocytes. *Leupocenia therefore is present.* The hæmoglobin was not determined—the blood was of a good colour. Its coagulability was markedly increased. A differential leucocyte count was made with the following result :—

Eosinophiles	11·6	per cent.
Polymorphs	57·4	,,
Mononuclears	4·2	,,
Large lymphocytes ...	8·6	,,
Small lymphocytes ...	16·2	,,
Transitionals	2·0	,,

With the exception, therefore, of a *marked eosinophilia*, the result probably of infection with *metazoan parasites*, so common in these fellaheen, the count was normal. No protozoal parasites of any kind were found.

Very different was the differential count in blood taken at the same time from the growth on the neck. It gave:—

Eosinophiles...	2·2	per cent.
Polymorphs	26·8	,,
Mononuclears	23·6	,,
Large lymphocytes	40·8	,,
Small lymphocytes	3·2	,,
Transitionals	3·2	,,
Basophiles	0 2	,,

There were many free nuclei of disintegrated mononuclears. Here, then, we find a marked increase of the larger mononuclear cells at the expense of the polymorphs. The blood was taken by means of a fine capillary pipette thrust through a small needle puncture into the depth of the growth. This slight operation was not unattended with pain, the patient wincing and complaining.

Before going further, it is interesting to compare these results with those obtained by CARDAMATIS[1] in several cases of oriental sore in Greece. In three cases he took blood from the finger and from the congestive zone at the periphery of the lesions. His counts are not at all unlike those recorded above, and he found in the blood from the congestive zone the same marked increase of large mononuclear elements as we record in the case under discussion. Indeed, as regards this third case, the counts are almost identical. As mentioned, blood taken from the growths by puncture and made into films in the usual way, when fixed and stained by the Leishman method, showed parasites belonging to the genus Leishmania. It was thought advisable to examine the contents of nearly every one of the growths. It will be best to consider these briefly in detail.

1. *Face growth.*—Parasites numerous, both free and in the mononuclears. None seen in the polymorphs. Many of the mononuclears are crowded with them, thirty being no uncommon number in one cell. Some of these mononuclear cells are very large with much extra-nuclear protoplasm, and are evidently the large endothelial cells commonly found infected in cases of kala-azar and Oriental sore. The free parasites occur singly, in pairs and in the larger groups which have been so often described by various observers. As many as 12 lying in close apposition counted in one clump. The blepharoplasts are both rod-shaped and spherical. Single, somewhat large forms with curved blepharoplasts noted. In addition, there are small coccoid bodies which may be free nuclei or special parasitic forms, and there are also somewhat pear-shaped or wedge-shaped cells staining a light rose pink, and exhibiting each a small spherical nucleus, but no blephoroplast.

2. *Neck growth.*—The parasites are not so numerous as in 1. They show vacuoles better, and occur both free and in the mononuclears (*Fig.* 5). Curved blepharoplasts were again noted in some of them. Blood and white cheesy matter mixed were also obtained from this growth, kept in a sealed, sterile capillary tube for six hours at room temperature (about 35° C.), and then smeared and stained. Parasites were found free and in mononuclears, and groups of what seemed to be large cocci were observed, as was a number of pale blue homogenous, structureless masses with regular outlines, probably formed from the matrix of ruptured host cells.

3. *Left upper arm growth.*—Parasites fairly numerous. Coccoid bodies and pink pyriform and wedge-shaped cells present. Small clumps comparatively common. A large

cell noted which stains a pale blue and contains a faint indication of what may be a large nucleus, although the latter stains more faintly than the cell protoplasm. Similar large blue cells have been seen in splenic smears from cases of kala-azar.

4. *Left forearm growth* (subsequently excised).—Serum and a little blood was obtained. There were many parasites in the mononuclears. Cells like degenerated leucocytes present.

5. *Right shoulder growth.*—Large numbers of parasites both free and in the mononuclears. Free clumps well seen. Degenerated white cells noted.

6. *Right upper arm growth.*—Parasites very numerous, and are more spherical in shape than in the other films. Mononuclears crowded with them. Vacuoles well marked. Rod-shaped, curved and spherical blepharoplasts. One form noted with two nuclei, a well-marked vacuole and a single curved blepharoplast. This possibly represents a dividing parasite. Some very curious masses observed either the result of fusion or of division. A small accessory growth situated close to the main tumour also showed the parasites.

7. *Growth on back.*—A film made from the content, of this small growth showed no parasites.

8. *Thigh growths.*—From these tiny tumours only white cheesy sebaceous-like matter was obtained. Films were made of it, and coccal forms of two kinds were found—one resembling those seen in the smears of similar material from the neck growth and taking on a deeper stain than the other, which consisted of small cocci of the usual type, occurring largely as diplococci.

Morphology of parasites.—For the most part the parasites conform to the typical *Leishmania tropica*, but

will probably require special and detailed description. Practically all the forms which have been described in oriental sore are present, but careful examination will be necessary in case differences, either in structure or arrangement, exist.

At present we need only mention the curved blepharoplasts which struck us as peculiar and the bodies staining a rose-pink. Examination of sections stained with eosin and haematoxylin showed these latter to be plasma cells.

The special form of large cocci found in the growths containing no Leishmania and in the cheesy matter from the neck tumour also claim attention. They are 4 to 6 times the size of the small cocci present, and tend to stain very feebly at their centres. Indeed, some of them present centrally placed unstained areas. They may occur in clumps or in pairs, and then may resemble in some measure huge gonococci. It is not likely that they are concerned with the Leishmania infection save in the way of symbiosis. CARTER[2] has pointed out that *L. tropica* grows best in culture when associated with masses of cocci and bacteria.

Although the suggestion as regards the origin of the blue homogenous masses may be correct, it is curious that many of them are very regular in outline, spherical or oval, and resembling, as one may say for want of a better term, " washed out " lymphocytes whose nuclei have vanished.

The white cheesy matter is no doubt sebaceous in origin.

Histo-pathology of growths.—The first growth excised was a small one, accessory to that on the left forearm, subsequently removed.

The tissue was fixed in formol alcohol, hardened in alcohol, cleared in xylol, imbedded in paraffin and, after the usual treatment stained in a variety of ways. The earlier sections were slightly thick, and at first glance exhibited all the appearance of a squamous carcinoma of the skin. The most prominent feature is the presence of numerous typical cell nests (*Fig. 6*) which, according to LAZARUS-BARLOW[3] may, for all practical purposes, be taken as diagnostic of that condition. Leaving the clinical history out of account, however, it was soon evident that we were not dealing with a malignant growth. There is an increase in the rete Malpighi, long branching columns of which stretch down into the underlying tissues (*Fig. 7*), but there is no actual invasive process, and there are no isolated masses of prickle cells. In these respects the condition resembled a papilloma.* The cell nests, however, are most typical. At the centre of one of the nests (*Fig. 8*) there is a clear glistening oval body about 28μ by 18μ, containing numerous grains of what is undoubtedly pigment. It is evident that there has been a hyperchondrifraction of the stratum corneum, as the body stains in the same way as the horny layer, giving rise to this curious appearance, an appearance not unlike a large molluscum body but clearer, more glistening and as mentioned, studded throughout with pigment. It is known that in the negro's skin pigment granules may be traced from the stratum granulosum to the outermost layers of the stratum corneum. The same is no doubt true, though to a less extent, of the Egyptian. The cells

* It is worthy of note that BITTER & FERGUSON, in Egypt, have recently discovered a species of *Leishmania* in *ulcerated* papillomatous lesions on the limbs of Egyptian fellaheen. (See paper by DAY and FERGUSON in *Ann. Trop. Med. and Paris.* Vol. III. No. 3. *Nov. 1st, 1909*).

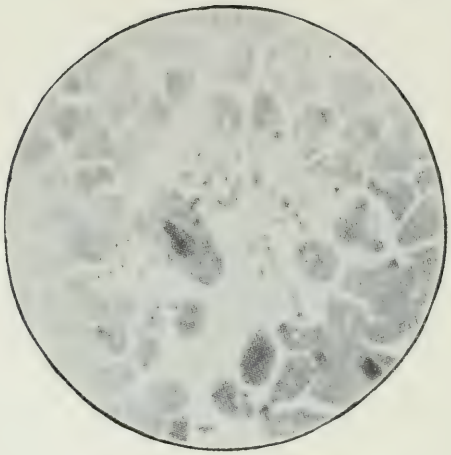

Figure 5.

Parasites free and grouped together in the cytoplasm of a large mononucleated cell, the oblong nucleus of which alone shows distinctly. (Page 113).
Magnification about 700 diameters.

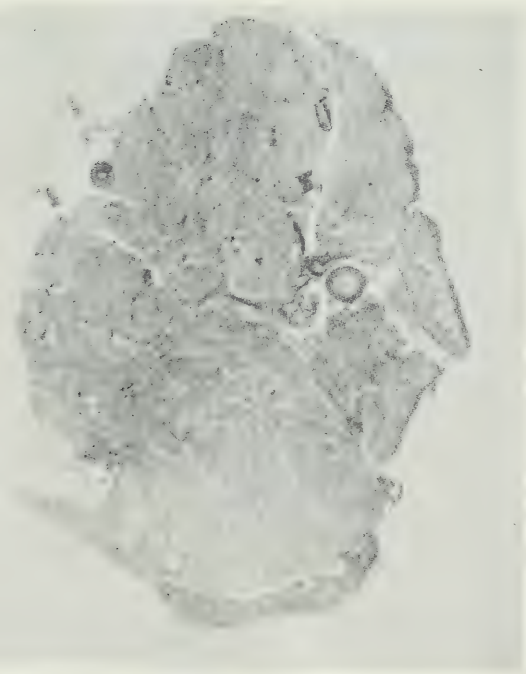

Figure 6.

Section of small growth first removed, showing cell-nests and cellular invasion of the rete Malpighi. (Page 116).
Magnification, 21 diameters.

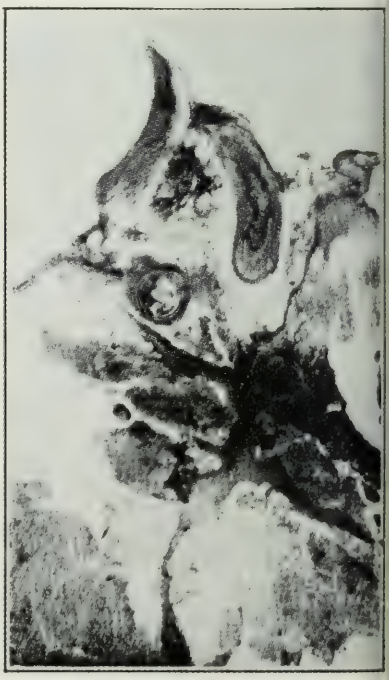

Figure 7.

Section of small growth first removed, showing proliferation of the rete Malpighi. (Page 116).
Magnification, 50 diameters.

Figure 8.

Cell-nest, showing pigment in central inclusion. (Page 116).
Magnification about 100 diameters.

Figure 9.

Section of second growth excised, showing downgrowths of rete.
The cellular infected layer is well seen. (Page 122).

of the rete show marked perinuclear vacuolation, while the papillary layer of the skin is hypertrophied, or at least appears to be so, invading and even cutting off and disintegrating portions of the rete, while itself invaded by infiltrating cells. There are islands of cellular tissue studded about in the mass of the prickle cells (*Fig. 6*). In these earlier sections the sub-epidermic tissue presents the appearance of a cellular connective tissue undergoing inflammation and some proliferation, and does not apparently conform to the descriptions in English text books and papers of sub-epidermic tissue in oriental sore, albeit examination with high powers of the microscope showed that the cytoplasm of numerous large cells with vesicular nuclei was full of Leishman bodies. These showed up best in sections stained by Van Gieson's method or by hæmatin. Free parasites were also visible in the dilated capillaries, in mononuclear leucocytes lying amongst the cells, no doubt as a result of diapedesis, and between the cells themselves, presumably in the serofibrinous effusion. Some of the smaller vessels in this tissue showed distinct endarteritis.

At this stage one may quote the description given by FORDYCE[4] of the histo-pathology of multiple benign cystic epithelioma. He says that under the microscope the tumours are seen to be "made up of irregularly rounded, oval and elongated masses and tracts of epithelial cells, corresponding to those in the lowermost layer of the epidermis, and in the external root-sheath of the hair-follicle. The epithelial masses may be distinct or made up of inter-communicating bands and tracts, in some places resembling coil-ducts. *Cell "nests" are met with as in malignant epithelioma, enclosing horny, granular and colloid tissue.* Colloid degeneration of individual

cells is also encountered in the cell masses. The connective tissue about the cell collections is somewhat condensed, but is not the seat of any inflammatory process."

It must be confessed that for the most part this description applied very well to the earlier sections studied, and it was found that ALLAN JAMIESON,[5] quoting various authorities, speaks of epithelial cystadenoma as a species of acanthoma, while the description he gives does not differ markedly from that stated above.

It will perhaps be interesting also to consider some of the latest utterances in English or American text-books on the histo-pathology of true oriental sore.

MANSON[6] says little—" Section of the papule displays an infiltration of the derma by a mass of small round granulation cells. These lie between the elements of the tissues, particularly about blood-vessels, lymphatics and sweat-glands; towards the centre of the lesion they completely replace the normal structures."

WRIGHT,[7] in his original paper, states that " the lesion consists essentially of a very extensive infiltration of the corium and papillæ by cells, accompanied by atrophy and disappearance of the epidermis of the part. The infiltrating cells are plasma cells, various kinds of lymphoid cells, and large cells with single vesicular nuclei, and a relatively large amount of cytoplasm, in which are large numbers of the micro-organisms. These large cells, over extensive areas, are very numerous, and constitute the principal part of the infiltration. They are regarded as proliferated endothelial cells."

BROOKE[8] mentions the researches of Carter, Reihl, Leloir, Unna and Kuhn, "who all found it to be a chronic sero-fibrinous inflammation. There is a round-celled infiltration of the skin and subcutaneous tissue.

In the centre of the nodules this infiltration is so dense that the tissue elements are entirely disintegrated. The lymphatic vessels are dilated and there is much œdema. Necrosis proceeds in the centre of the infiltration tissue. There is cornification of the hair root-sheaths, preventing a subsequent new growth of hair at the spot. There is endothelial proliferation of the blood vessels, often leading to their entire obliteration."

CHRISTOPHER and STEPHENS,[9] in their latest edition, do not deal with the subject, nor does DANIELS.[10] The English translation of SCHEUBE'S[11] work has a passage much like that in Brooke's book:—

"There is an infiltration of the skin and subcutaneous tissue, with small round oval cells, multi-granulated and giant cells, and also a few leucocytes. In the centre of the nodules, over which the epithelium is attenuated, the infiltration is so dense that the tissue elements are entirely disintegrated, while towards the periphery the cells form small centres, mostly situated in the vicinity of blood vessels and lymphatics and sweat glands. The lymphatic vessels and spaces are uncommonly wide, and there is œdema. In the centre of the infiltrated tissue, small necrotic particles are enclosed, and this, when the sections are stained, exhibits large fibrinous contents: the tissue otherwise also contains much fibrin (Unna). Those hairs that still exist are, according to Kuhn, partly broader, partly narrower, occasionally ravelled, and they always exhibit a granular appearance. The root-sheaths are sometimes dilated. Here and there the inner root-sheaths, and to a great extent the outer root-sheaths, are also transformed into a shiny mass, probably cornified. In the connective tissue around the hair follicles, cavities are found filled with shiny flaky masses which, according

to the way they are cut on section, appear of a round or oval form. In consequence of the cornification of the root-sheaths no new growth of hair is possible. The blood vessels exhibit endothelial proliferation, which may lead to their entire obliteration."

FIRTH,[12] in Allbutt's "System of Medicine," has quite a lengthy description as follows:—

"The histology of these sores has been thoroughly worked out; and, if sections be made of the initial papule before ulceration, no difficulty is experienced in demonstrating that the whole thickness of the skin and subjacent tissue is infiltrated with lymphoid and epithelioid (mesoblastic) cells, accompanied by more or less complete disintegration of the normal tissue-elements thereby. In the centre of the papule the infiltration by young round cells is so complete, that little can be seen of the sweat-glands. Towards the edges of the diseased area, the new cells occur in isolated clusters or groups, chiefly round blood-vessels or lymphatics. The infiltration does not seem primarily to involve either the hair-follicles or the sebaceous glands. The individual cells of this infiltration vary from 7μ to 9μ; their nuclei from 5μ to 6μ; the nuclei are large, generally single, but in parts multiple. The anatomical structure of the papule and surrounding skin indicates that oriental sore is of the type of a granuloma; in fact the most elementary microscopical examination of the lesions show that it is a reaction of the skin against some virus of low virulence, which has produced granulomatous changes in the corium beneath and round the ulcer. So chronic are the changes which are sometimes met with, that a close resemblance to tuberculosis may be occasioned. It is important to bear this in mind, because it has several times been suggested that certain of these

lesions are tuberculous. Doubtless, syphilitic and tuberculous ulcers have from time to time been placed in this group, but that there is an entity to which the term oriental sore is applicable, which is due to some virus different from syphilis and independent of tubercle bacilli, seems certain."

JACKSON,[13] on the other hand, states that the pathological anatomy of tropical ulcer needs to be cleared up by further study. None of these accounts, it will be seen, mention the presence of cell nests, or even the increase in the rete malpighi, which was so marked a feature in the sections of the small growth first studied. We were inclined to ask if this tumour was taking on malignant features, if it was a true oriental sore in the papular stage, or if these descriptions referred only to the ulcerative stage of the lesion. Manson's brief statement, however, distinctly mentions section of the *papule*.

Another and larger growth of four months' duration, that on the outer surface of the left forearm, was excised and examined. After excision, blood was taken from the cut surface, but no parasites were found in it, nor were they present in blood stained serum, obtained by thrusting a capillary pipette through this surface and some distance into the tumour mass. This is a point of some interest.

Thin sections were made of the growth and stained by Leishman's method, with Heidenhain's iron-hæmatoxylin, with hæmatin, Van Gieson's stain, eosin and methylene blue, hæmatoxylin and thionin blue, and following NATTAN-LARRIER and BUSSIÈRE[14], with carbol-thionin.

The appearances presented by these sections were much more like the description quoted. There was not nearly so great a proliferation of the rete malpighi, though here

also, in some parts, a tendency to down-growth and to the formation of cell-nests was noted (*Fig. 9*). A study of the sections stained with eosin and methylene blue, however, showed that the cells present in the sub-epidermic layer, answered very closely to those mentioned by Wright. Indeed all the classical signs were to be observed, and there could be little doubt that the condition was identical with that found by many observers. In these sections there were not, as a whole, nearly so many parasites as in those of the small growth first examined, and they seemed to be confined to the endothelial cells and the mononuclears. In certain areas, however, sections stained with carhol-thionin and carefully differentiated with spirit, showed a heavy infection of the cells. (*See slide*).

At certain points the infiltration of the epidermic layers by the round-celled growth was evident, but at most points there still persisted a considerable layer of the rete.

We could find no evidence of actual necrosis, nor were giant cells visible. It was not until we consulted the recent French work on tropical medicine by JEANSELME and RIST that we found a description of anything like the condition seen in the sections of the first small growth observed. There, however, we came across an excellent account of the histo-pathology of "Bouton d'Orient." These authors state that the dominant change consists in a thickening of the rete malpighi (hyperacanthos and an incomplete keratinization of the corneal layer (parakératose). The prickle cells are separated one from the other by an interstitial œdema and perninuclear vacuolation occurs. They go on to describe the state of the sub-epidermic tissue in much the same way as other writers, but lay stress on the foci of necrosis and the presence of giant cells. Their diagrams, both of skin sections and of

the periphery and centre of a typical inflammatory nodule, are very instructive, and save for the absence of cell-nests and the presence of the giant cells might apply to our sections of the small growth first removed and studied.

It is then we think evident that the skin disease under consideration is an example of what is called oriental sore, but it appears to be a type not prone to ulceration.* In this case some of the growths have been present for two years, and even when punctured tend to scab and heal immediately.† In the father's case the tumours have persisted unchanged, save as regards size, for six years, in the sister's case for four and a half years. The patient has been very closely questioned on these points and is very definite in his reply.

Has such a condition been previously reported? With one exception we can find no record of such being the case. Some writers speak of the papules persisting for a long period (CARDAMATIS[15] mentions one of two and a half months) and others of chronic papules which abort, but in no instance is any indication given that growths may attain the size they have done in this case without showing any sign of breaking down.‡

The exception mentioned is given by CAMBILLET,[16] who recently described the case of a small native boy in Algiers, who presented on the right cheek a tumour,

* Is it not possible that the result depends upon the reaction of the tissue to the virus? If this be strong the epidermic layers thicken; if weak they are destroyed. It may be so or special forms of Leishmania may produce their own specific results; or again, symbiosis, with cocci or bacteria may play a part.

† A portion only of the small growth showing the cell-nests was excised. The wound healed rapidly, and now the nodule presents much the same aspect as it did before part of it was removed.

‡ See, however, note at end of this paper.

which, to judge from the photograph given, must be almost identical with the face growth in our case. It commenced as a small papule, increased in size until, at the time the paper was written, it measured three centimetres in diameter, and showed no sign of ulceration or discharge. It had persisted for a year in this state. On puncture it yielded blood and "*de petits grumeaux blancs*," and in smears *Leishmania tropica* was found. He concluded that the case was one of "Bouton d'Orient," and certainly this term is much more applicable to his case and ours than that of oriental sore. The latter, in any case, is a misnomer, as instances have been described from Bahia by JULIANO MOREIRA, and recently from Bauru in Brazil, by LINDENBERG,[17] who found Leishman bodies present. His work has been confirmed by CARINI and PARANHOS.[18] We think cases of this kind might, with advantage, be termed Leishman nodules, as the word nodule sufficiently describes the growth, and practically all are agreed that *L. tropica* plays a part, and probably the chief part, in their etiology. It is true that some are apparently anxious to abolish the term *Leishmania* as applied to the parasite altogether and substitute for it *Crithidium* or *Herpetomonas*, but the word is now so familiar, and in such general use that it might, with advantage be retained and applied in its modified form as above indicated. Apart from what has been said there is other evidence pointing to this case being one of Leishman nodules.

1. The condition is known to occur in Egypt.

2. Exposed parts of the skin are chiefly affected, the Egyptian fellah being accustomed to work stripped to the waist.

3. The coagulability of the blood is increased; markedly so.

CARTER,[19] however, points out that in oriental sore more than one person of a family or household is rarely or ever attacked while, as already mentioned, our second case, about to be described, appears undoubtedly to have derived his infection from the first, two of whose family also suffered from the disease. GROS,[20] who has published an account of four cases on the Algerian littoral is of CARTER'S opinion. In no instance was infection transmitted from his cases to those in contact with them. How close this contact is likely to have been, anyone conversant with Eastern customs and usuages knows. GROS concludes that *le bouton d'Orient parait donc peu contagieux.*

The account of our second case is therefore likely to be all the more interesting.

Case II.—Yani Suleiman; aged 21. Soldier in No. 4 Company, 16th Battalion, Egyptian Army, an Egyptian fellah from the village of Ben Abied, in the Mudirieh of Minieh, Upper Egypt. He is a sturdy son of the soil, well-nourished and more intelligent than his compatriot. He enlisted on the same day as did Case I., and for the last five months the two men have been eating together, and sleeping side by side, while they are in the same section of the same company every parade. Patient denies having ever worn the clothes or boots of Case I.

Admitted October 30th, with growths very like those in Case I., situated on his left thigh, right knee and left foot. On admission he was noticed also to have a small abscess below the outer canthus of his left eye. This contained pus and was evacuated. It may be said at once that no *Leishmania* were found in the pus.

Family History.—Unimportant. Nothing of interest.

Personal History.—Patient states that as a small child

he was possessed of an evil spirit for a year, but otherwise has always been healthy. No venereal history obtainable and no signs of venereal disease.

History of present illness.—The first growth on the anterior surface of the left thigh appeared four months ago, *i.e.*, one month after he came into contact with Case I. A second lesser growth, now absorbed into the first, appeared about the same time as did a third growth, accessory to the fused first and second. A fourth on the inner surface of the right knee is three months old, and so is a fifth on the dorsum of his left foot about half an inch from the bases of his first and second toes. The tumours itch and are painful on pressure.

Clinical Examination showed the patient to be perfectly healthy, with the exception of the skin lesions. These are of the same type as in Case I. When punctured they yield blood only, and films of this blood show in every instance *L. tropica*. Those however are not nearly so numerous as in Case I. The greatest number was found in the knee growth. They occur both free and in the mononuclears, and present no special features. A good many of them appear to be smaller than those in Case I. The tumours show no tendency to ulceration and quickly heal under a scab after being punctured. Blood from the skin covering the growths shows no parasites.

The measurements of the growths are as follows :—

On the thigh (1 & 2 combined) ...	17 mm. by 12 mm.
On the thigh accessory... ...	7 mm. by 7 mm.
On the knee	10 mm. by 10 mm.
On the feet	5 mm. by 5 mm.

Blood Examination.—The blood coagulates very rapidly. A blood count made by Captain ENSOR on November 2nd,

showed 4,700,000 red blood corpuscles and 16,000 leucocytes. It will be remembered that the patient at this time had a boil on his face, probably the cause of the leucocytosis. After a week the leucocyte count dropped to 12,000, although the patient was being treated by Captain ENSOR[21] with tincture of senega, according to his method in kala-azar cases. As he was anxious to test the effect of the drug the case was handed over to him and has not been studied so fully by us as was Case I. It is chiefly of interest in that it is an example of the transmissibility of the disease and, apparently, of the same type of the disease. What was the agent of transmission? Was it a bed bug? This is perhaps the most likely insect; for bugs, *C. lectularius*, are a common pest in barracks tenanted by Egyptian troops. Next most likely is a *Phlebotomus*, said by PRESSAT,[22] to be blamed by the felaheen in Egypt, and regarded by SERGENT and others as a possible vector.

This and other questions we would leave to a later paper, and conclude by thanking Captain ENSOR, S.M.O., Khartoum, for help in connection with the cases, and Dr. BEAM for the trouble he took to secure good photographs of these interesting skin lesions.

NOTE.—Since this paper was written a second article,[23] by CARTER, has appeared, in which he draws attention to the various types of oriental sore which exist in India, mentions a non-ulcerating form, apparently not identical with that we have described, and like us, takes exception to the term oriental sore, though without putting forward any substitute. He also refers to the possibility of there being different varieties of Leishmania, an observation with which we wholly agree, and in the light of which we hope to study the parasites found in the skin lesions described.

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PRELIMINARY NOTES ON THREE NEW SPECIES OF TONGUE-WORMS *(LINGUATULIDÆ)*,

IN THE COLLECTION OF THE "MUSEUM D'HISTOIRE NATURELLE," PARIS,

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The collection of Tongue-worms (Linguatulidæ) belonging to the Paris Natural History Museum, which was handed over to one of us for the proper determination of its material, contains three new and interesting species of which we beg to submit a short preliminary account.

Unfortunately, two of these species are founded on single and very poorly preserved specimens; their description is, therefore, necessarily incomplete with regard to certain details, but sufficient none the less to permit of the establishment of perfectly distinct new species.

The first species we propose to call *Porocephalus bouvieri*, dedicating it to Prof. BOUVIER, the distinguished entomologist of the Paris Natural History Museum. It was found by Prof. VAILLANT in the Congo in 1896, and is mentioned on the annexed label as taken from the stomach of an *Heterolepis savorgnani*, a snake from the French Congo, which has been identified by Mr. BOULENGER with *Simocephalus capensis*.

This porocephalus, with its large cylindrical body of almost uniform thickness throughout its length, with annulations hardly perceptible or entirely obliterated, with the closely packed uterine coils clearly visible through the

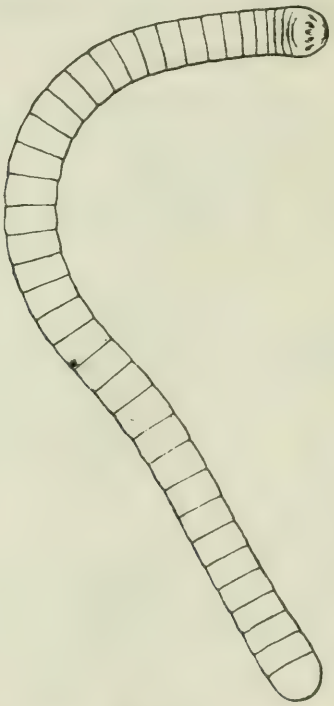

Figure 1.
Porocephalus bouvieri. n. sp. ♀.

thin, transparent body wall, very strikingly resembles certain Neotropical species of frequent occurrence in the lung and trachea of the Ophidia of the genera *Boa*, *Lachesis* and *Crotalus*.

The single specimen in the collection is an adult female measuring 60 mm. in length. Its body is almost cylindrical in shape, with a maximum diameter of

about 3 mm. It tapers slightly towards the anterior extremity, and is largest at the rounded posterior end which terminates abruptly as if truncated. The body annulations, from 1 to 2 mm. wide, are so very indistinct that it is not possible to indicate the exact number. There seem to be 38 to 40. Through the thin body wall may be seen the straight alimentary tube and the tangled coils of the uterine tube filling the entire body. The cephalothorax measures 3 mm. in length and about 3 mm. in width; it is bluntly rounded anteriorly, convex on the posterior aspect, slightly flattened on the ventral side. The mouth and hooks are arranged in a slight convex arch close to the anterior margin. The mouth is more or less pear shaped, and measures 0·31 mm. in length by 0·15 mm. in width. Its anterior pole is almost on a level with the upper ends of the inner hookpits. The proximal hooklets are single, each consisting of a stout, strongly curved chitinous process 0·5 mm. in length; the outer ones are double. Of the geminate hooklets, one, the principal, is similar in size and shape to the single inner hooklets, the accessory, placed immediately above the principal, is very slender, only slightly bent, and measures 0·37 mm. in length.

Both the anus and the vagina open close together at the posterior extremity. The fully-developed ova measures 0·080 mm. in length and 0·067 mm. in width; they are surrounded by a hyaline envelope measuring 0·128 by 0·120 mm.

The second species we propose to call *Porocephalus joubini* in honour of Prof. JOUBIN, of the Paris Museum. In general appearance and in the arrangement of its mouth and hooklets at the narrowed anterior region of its cephalothorax, it resembles the linguatulid of the

Common Caiman *(Caiman sclerops)* described by DIESING in 1835 under the name of *Pentastoma oxycephalum*, but it differs from it on account of its much larger size: our specimen measures 42 mm. in length, and its diameter over 4·5 mm. at the anterior extremity and 3·5 mm. at the posterior end, whilst the largest specimen of the Neotropical species measures, according to LEUCKART, 25 mm. in length and 3·4 mm. in maximum diameter.

Porocephalus joubini was found in the nasal cavity of the Siamese Crocodile (*Crocodilus siamensis*), which inhabits Siam, Cambodia and Java; a zoo-geographical area very different to that of the hosts of DIESING'S species the Common Caiman (*Caiman sclerops*) and the American Crocodile (*Crocodilus americanus*) which inhabit South and Central America respectively.

The mouth of *Porocephalus joubini* is suboval, the hooklets are very small and arranged at the corners of an isosceles trapezoid, the wide base of which, limited by the outer hooks, is at the level of the mouth. The short base, formed by the inner hooks, is situated considerably above the mouth opening. The single specimen being a fully mature female, the body annulations are completely effaced. The posterior extremity is obtuse, the anus is terminal, the ova measure 0·060 mm. by 0·050 mm.

Porocephalus boulengeri, n. sp., anterior extremity of female.

The third species was found in 1906 within the peritoneal cavity of a Gaboon Puff Adder (*Bitis gabonica*). Other identical specimens were found by one of us in the trachea of a Common Puff Adder (*Bitis arietans*) that died at the London Zoological Gardens in 1907. We propose to give it the name of *Porocephalus boulengeri*, in

honour of Dr. G. A. BOULENGER, the eminent herpetologist of the British Museum.

Our mature female specimens measure from 35 mm. to 45 mm. in length. The body is elongate, fusiform and slightly curved ventrally. The annulations are almost effaced, there appear to be about thirty. The posterior extremity is bifurcated, and the anus opens between its two slender branches. The cephalothorax is triangular in shape, and measures 1 mm. to 1·5 mm. in length, and 2 mm. in width at its base. The mouth presents the outline of an inverted thimble, and opens on the ventral surface of a prominent rounded lobe formed by the incurved anterior extremity of the cephalothorax. Posteriorly to this lobe are the four hooklets arranged in the form of a trapezoid with small base anterior, and formed by the inner hooklets and the wide base considerably lower and formed by the outer hooklets. Each hooklet is simple, and presents at its base two prominent vesicular protuberances. The outer hooks measure 0·31 mm. in length, the inner ones 0·24 mm. The eggs are oval in shape, and measure 85μ × 70μ.

This species greatly resembles a linguatulid of the Neotropical region, described by DIESING in 1835 under the name of *Pentastoma furcocercum*,* from specimens found by NATTERER in the lungs of the White Amphisbæna (*Amphisbæna alba*) and in the body cavity of the following snakes: *Drymobius bifossatus*, *Zamenis constrictor* and *Boa constrictor*. But it differs from it in certain characters, such as larger dimensions, single instead of geminate

* In 1850, DIESING changed the name *Pentastoma furcocercum* into that of *Pentastomum bifurcatum*, and SHIPLEY (1893) mentions this species under the name of *Porocephalus bifurcatus*. However, in accordance with the rules of Zoological nomenclature, the older specific designation must have precedence.

hooklets and fewer annulations. However, as suggested by LEUCKART, DIESING'S specimens may have been immature, hence, possibly, the smaller dimensions and the geminate hooklets. With regard to a difference in the number of rings between the two species we are uncertain. In our specimens there seem to be from 25 to 30 rings, but unfortunately the body annulation is not very distinct. DIESING'S picture (Fig. 25 in Plate IV of his Monograph) of 1835 shows about 100 rings. In the revised description, published in 1864, he mentions about 40 rings. Finally, with regard to geographical distribution, a difference of realm is a powerful argument in favour of diversity of species. The known definitive hosts of both *Porocephalus furcocercus* and *P. boulengeri* are species peculiar to their respective regions. Indeed, Africa and America posses no reptilian species in common, and the three American genera of snakes mentioned as hosts of *Porocephalus furcocercus* have no representatives in Africa. We believe, therefore that, notwithstanding great structural similarity, the Ethiopian new species *P. boulengeri* must be regarded as distinct from the Neotropical species *P. furcocercus*, DIESING.

The paper I have just read, and which I had the honour of preparing with Professor VANEY, during a few very pleasant hours we spent together in his laboratory at the Faculté des Sciences, in Lyons, needs some comments.

In the first place, when we state that *Porocephalus bouvieri*, in general appearance, resembles certain common tongue-worms of the Neotropical snakes of the genera *Boa*, *Lachesis* and *Crotalus*, we purposely avoid

mentioning the name *Porocephalus crotali*, hitherto applied to designate collectively the linguatulids peculiar to these ophidians, because, in the course of my investigations on this very interesting group of the Acarina, I have found that, under the name *Porocephalus crotali*,

Figure 2.

Porocephalus clavatus (WYMAN)?

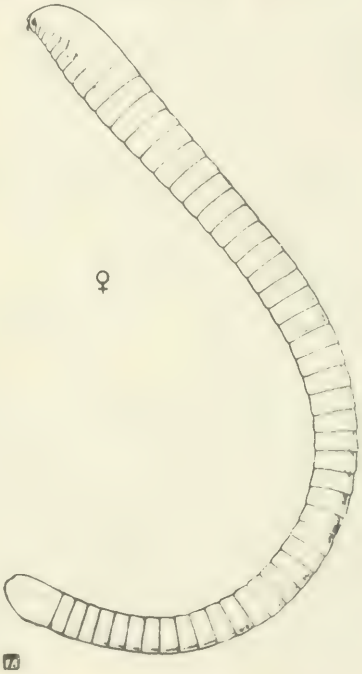

Figure 3.

Porocephalus stilesi n. sp.?

at least four different species have been confounded. The tongue-worms of the Boas differ from those of the venomous snakes of the genus *Lachesis*, and both differ from those of the Rattle snakes, and again from those of the large South American lizard, the Great Teju *(Tupinambis teguixin)*.

In a complete monograph of the Linguatulidæ, which I hope to be able to publish very shortly, I have described as fully as possible the characteristics of each species. Now, I will not trouble you with minute structural details; but, in showing you some of my specimens and drawings, I must mention one very valuable distinctive character which may be recognised almost at a glance, and that is the number of the body rings, which is different in each species. The porocephalus of the Common Boa *(Boa constrictor)* presents from 35 to 38 annulations, the species peculiar to the Curucucu or Bush-master (*Lachesis mutus*) and to the Rat-tailed Serpent or Fer-de-lance (*L. lanceolatus*) presents from 45 to 50 rings; the species discovered by HUMBOLDT in *Crotalus terrificus** has over 80 annuli,† so

*In his "Ansichten der Natur" (p. 162, 1st ed., 1808), ALEXANDER VON HUMBOLDT mentions the host of his new parasite as "Tropical Rattlesnake." In the notes to the same work he names it *Crotalus durissus*. Three years later, in the "Recueil d'Observations de Zoologie et d'Anatomie comparée," which he published with BONPLAND, he makes a new species of the Cumana rattler, and calls it *Crotalus cumanensis*. Doubting that the North American Rattlesnake *Crotalus durissus* could be the Cumana host of HUMBOLDT'S tongue-worm, and not being able to find the specific designation *cumanensis* in any of the catalogues of the American Rattlesnakes, I consulted Mr. BOULENGER, of the British Museum, and he told me that HUMBOLDT'S *Crotalus cumanensis* is without doubt *Crotalus terrificus*, LAUR.

†DIESING (1835), under the name of *Pentastoma proboscideum R.*, states that in small female individuals taken from the body cavity and lungs of a rattlesnake (*Crotalus horridus*) the body presented numerous and closely set rings. Further, under the name of *Pentastoma subcylindricum*, he describes a nymphal linguatulid, with over 80 annuli, found by NATTERER in the organs and body cavity of the Murine Opossum (*Marmosa murina*) and other Brazilian mammals. This may possibly be the nymphal form of the species first described by HUMBOLDT under the name of *Porocephalus crotali*. The relationship between DIESING'S species *Pentastoma subcylindricum (sensu latoire)* and *Porocephalus crotali (sensu latoire)* was first suggested by JEFFRIES WYMAN (1847), more definitely stated by

far, at least, as I can judge from a badly preserved female specimen in the collection of the Paris Museum.

In accordance with these facts, we must necessarily restrict the use of the name *Porocephalus crotali* to the species found in *Crotalus terrificus*, *C. horridus*, *C. adamanteus*, and other Rattle snakes. For the linguatulid of the Boas, we are bound to adopt the name *Porocephalus clavatus*, suggested, as far back as 1845, by WYMAN (1847) who first described this species and said: "If it should prove to be a new species I propose the name of *Linguatula clavata*." For the species found in the Bush-master (*Lachesis mutus*) and the Fer-de-lance (*L. lanceolatus*), I propose the name of *Porocephalus stilesi*, in honour of the learned American helminthologist, Dr. WARDELL STILES, who, in 1891, gave us a masterly paper on the linguatulid of *Boa constrictor*. Finally, for the tongue-worm of the Great Teju, which I have not been able to examine myself, but which, judging from the drawings (*Figs. 1-10, Plate IV.*) in DIESING's monograph, and from the different Sub-order (Lacertilia) to which its host belongs, is certainly a different species, I propose the name of *Porocephalus wardi*, in honour of Dr. HENRY B. WARD, of Nebraska, another distinguished American investigator who has contributed to our knowledge of the linguatulidæ.

Professor LEUCKART (1860), and experimentally proved by Dr. WARDELL STILES (1891). LEUCKART, who found only 40 annuli in specimens from the liver of a Philander Opossum (*Calaromys philander*) obtained from DIESING himself, explains the latter's mention of 80 rings as a mistake, but DIESING'S monograph is illustrated by four plates of figures, carefully drawn by F. ZEHNER, and the figure 25 on Plate III., which represents an enlarged specimen of *Pentastoma subcylindricum* from the Murine Opossum, shows distinctly 79 rings. The discrepancy is possibly due to the confounding of two or more species.

Having shown that WYMAN'S *Linguatula clavata* is a good species, I must point out that, although I place his species in a different genus, the name *Pentastomum clavatum*, suggested by LOHRMAN, in 1899, for a linguatulid of the Egyptian Monitor *(Varanus niloticus)*, cannot be retained, because, in accordance with Art. 36 of the International Code of Zoological Nomenclature, "a rejected homonym can never again be used, even when the species is placed in another genus." I propose, therefore, for the tongue-worm of the Egyptian Monitor the name of *Reighardia lohrmanni*.

Porocephalus joubini described by Prof. VANEY and myself should also be placed in the genus *Reighardia*. The genus, *Reighardia*, was established in 1899 by WARD for a linguatulid of Gulls and Terns first described, in 1861, by DE FILIPPI, who found a single specimen in the left air sac of a Common Tern *(Sterna fluviatilis)*, and again, in 1883, by MÉGNIN, from the Glaucous Gull *(Larus glaucus)*. WARD'S specimens belong, no doubt, to the same Holarctic or rather Arctatlantic species and were found in Bonaparte's Gull *(Larus philadelphia)*, and in a Tern common on Lake Erie. So far as I am aware, Professor WARD'S diagnosis of his new genus has not been published. The characters mentioned in the abstract of his paper, printed in the "Proceedings of the American Association for the Advancement of Science, Forty-eighth Meeting" (body elongate, transparent, and devoid of annulations; cuticula thin; mouth surrounded by a chitinous framework recalling that of the Sarcoptidæ), are insufficient, common to other genera, and one of them, the absence of annulations, erroneous. However, I believe Professor WARD is right in removing the linguatulid of Terns and Gulls from

the genus *Porocephalus* and making it the type of a new genus. I propose not only to retain the genus, *Reighardia*, but moreover, to include in it a number of other species the nymphal forms of which probably develop in fish. As external characters of the genus, I would suggest the following: Body cylindrical or spindle shaped; annulations, as a rule, very poorly developed and almost entirely obliterated in the mature female specimens; cephalothorax more or less tapering anteriorly, hooklets arranged as if at the angles of a trapezoid figure, the inner ones on a line anterior to and far in advance of the one on which the outer hooklets are situated.

In addition to *Reighardia sternæ*,* *R. joubini* and *R. lohrmanni*, I propose to include in this genus the following species: *Pentastoma oxycephalum*, DIESING, 1835; *P. gracile*, DIES., 1835; *Pentastomum platycephalum*, LOHRMANN, 1889; *Porocephalus indicus*, v. LINSTOW, 1908, and three new species, one of which I will briefly mention, because it is one of the most remarkable I have had the opportunity of studying. It was found by Dr. LEIPER in the lungs of a Nilotic Crocodile *(Crocodilus niloticus)* he shot at Fajao on the Murchison Falls, Victoria Nile. I propose to call it *Reighardia cincinnalis* to express by the

* DE FILIPPI (1861) gave no scientific name for this species, but merely mentioned it as the "*Linguatula della rondine di mare.*" DIESING was the first to give it a Latin name in 1864, calling it first *Pentastomum sternæ hirundinis*, and further in the same paper *Pentastomum sternæ*. MÉGNIN (1883), who received some specimens found in the air sacs of the Glaucus Gull (*Larus glaucus*), believing he was describing a new species, named it *Pentastomum lari*. Two of his specimens, collected by Professor POUCHET in Lapland, and now preserved in Professor BLANCHARD'S collection at the École de Médicine, Paris, are labelled *Pentastoma laponica*, MÉGNIN (1881), a name which I believe was never published. SHIPLEY (1898) mentions this species under the name of *Porocephalus lari*.

Latin term *cincinnus*, a curl or ringlet, the peculiar tendril-like spiral waving of the body of this linguatulid in its adult stage. The specimens examined by me are four adult females, varying from 108 to 124 mm. in length, by 3 to 4 mm. in maximum diameter. Their body is almost cylindrical—the ventral aspect is somewhat flattened. The posterior two-thirds are curled into a spiral of four to five rounds. The body annulation is visible only on the anterior third, from cephalothorax to first round, where from 60 to 62 rings may be counted. It is entirely effaced on the posterior two-thirds; the cephalothorax is almost triangular in shape, and measures about 2 mm. in length by 3 in width at its base; the hooks are single and arranged in such a way as to limit a trapezoid area between them, in the middle of which is situated the mouth.

The third species described by Prof. VANEY and myself under the name of *Porocephalus boulengeri* must, I think, be placed into a new genus together with DIESING'S *Pentastomum furcocercum* and the linguatulid found by DUJARDIN (1845) in the lungs of a Siamese gecko (probably *Gecko verticillatis)*, and named by DIESING (1850) *Pentastomum geckonis*. This new genus I propose to call *Raillietiella* in honour of the great French helminthologist Prof. A. RAILLIET of the Alfort Veterinary School. Its chief characters are: A bifid posterior extremity, three vesicular protuberances round each hook-pit, the female sexual opening at the anterior end of the abdomen.

I will now show you two lots of porocephali which appear to be exactly alike, but which, I believe, represent two distinct species. Both have been already described, one of them by LAMARE-PIQUOT, in 1835, and again by Dr. STEPHENS, in 1908; the other by DIESING, in 1850.

LAMARE-PIQUOT'S description was read at a meeting of the Paris Academy of Sciences, but does not appear to have been published in the Reports. However, a part of it, sufficient for diagnosis is given by LAMARE-PIQUOT in his "Réponse sur mon Memoire concernant les Ophidiens" (pp. 50, 51). It reads as follows: "This worm is to be found in the lungs and intestinal tube of the Demuha *(Coluber korros)*; it measures from 4 to 6 in. in length; its body is white and smooth, cylindrical in shape, and of the thickness of a medium quill pen; its head is globular, and twice as broad as the body. It is provided with four small hooks placed on either side of the mouth; these are retractile, composed of a horny substance, and measure about a quarter of a line in length. Between the head and the body there is a well marked constriction, which constitutes a regular neck, etc."

In his *Systema Helminthum*, DIESING (1850) mentions a linguatulid found by NATTERER, in Brazil, in the lungs of *Coluber lichtensteinii (= Drymobius bifossatus)* and, together with the one found by LEMARE-PIQUOT, in *Coluber (= Zamenis) korros*, which he considers to be identical, looks upon it merely as a variety of *Pentastomum proboscideum R.*, proposing the name *Pentastomum proboscideum* var. *coarctatum*. He gives the following very brief diagnosis: "*Caput basi coarctatum subhemisphæricum, subtus planiusculum, corpus annulato-plicatum v. læve.*"

In 1908, STEPHENS, obviously unaware of both LAMARE-PIQUOT'S paper and DIESING'S work, redescribed the Indian form from specimens found by Capt. PATTON in the lungs of the Indian Rat Snake *(Zamenis mucosus)*, and proposed for it the name of *Porocephalus pattoni*.

In 1908, in examining a small specimen of COUPER's snake *(Coluber corais*, var. *couperi* HOLBR.*)* that had died at the London Zoological Gardens, I found in its lung seven female specimens of a porocephalus answer-

Figure 4.
Porocephalus coarctatus. n. sp. ♀

ing DIESING's description of the linguatulid of *Drymobius bifossatus*. Later, through the kindness of Dr. STEPHENS, I was able to compare my specimens with those he had received from Capt. PATTON, and I found that, as I had surmised on geographical grounds, the Neotropical species differs from the Oriental one. In size,

in general appearance, in the peculiar shape of the cephalothorax, in the characteristic constriction which follows it, both species appear to be absolutely identical, but, while the Oriental species does not present more than 36 rings, the Neotropical one has 50 to 52. Here again the number of the body annulations presents a good and easily determinable specific character. I showed Dr. STEPHENS the part of my monograph concerning these tongue-worms, and when he read my suggestion that the Indian species named by him *Porocephalus pattoni*, would probably also be found in South China, owing to the presence of both *Zamenis korros* and *Z. mucosus* in that region, he handed me a bottle containing specimens of the same species collected by Dr. BELL in Hong Kong. I have also seen a specimen of this species in the collection of the Paris Museum, which was found in Luang Prabang, French Indo-China. Finally, Dr. FÜLLEBORN sent me a photograph of three specimens in the collection of the Hamburg School of Tropical Medicine which he states were found in an Indian snake. Thus, I have had the opportunity of examining a large number of specimens of the Oriental species from the most widely separated parts of its distributional area, and I have found them all exactly alike, and always presenting from 34 to 36 body rings. I hold, therefore, that the Oriental species named by STEPHENS *Porocephalus pattoni* is a good species, and differs from the South American one, which should be called *Porocephalus coarctatus*, raising DIESING'S designation from varietal to specific rank.

I will close my remarks by saying a few words on the species of *Linguatulidæ* which may occur in man.

Three different species have already been accurately determined, they are: *Linguatula serrata*, *Porocephalus armillatus*, and *P. moniliformis*.

Linguatula serrata,* being a parasite of some of our most important domesticated animals (dog, ox, sheep) has, as might be expected, a cosmopolitan distribution. In certain parts of Europe it is very prevalent. In its adult stage it is a parasite of the Dog *(Canis familiaris)*, the Wolf *(Canis lupus)*, the Fox *(Vulpes vulpes)*. In its nymphal stage it has been found in the following mammals: African Hedgehog *(Erinaceus æthiopicus)*, Long-eared Hedgehog *(E. auritus)*, Domestic Cat *(Felis catus)*, Black Rat *(Mus rattus)*, Brown Rat *(Mus norvegicus)*, Crested Porcupine (*Hystrix cristata*), Guinea Pig (*Cavia cutleri*), Common Hare (*Lepus europeus*), Common Rabbit (*Lepus cuniculus*), Horse (*Equus caballus*), Mule (*Equus asino-caballus*), Domestic Ox (*Bos taurus*), Bubal Antelope (*Bubalis boselaphus*), Blue Duiker (*Cephalophus monticola*), Domestic Goat (*Capra hircus*), Domestic Sheep (*Ovis aries*), Pronghorn Antelope (*Antilocapra americana*), Roebuck (*Capreolus capreolus*), Fallow Deer (*Dama dama*), Domestic Hog (*Sus scrofa domesticus*), Arabian Camel (*Camelus dromedarius*), Collared Peccary (*Dicotyles tajacu*).

*The synonymy of this species is as follows:—Adult form: 1787, *Ténia lanceolé*, CHABERT; 1787, *Ver rhinaire*, CHABERT; 1803, *Tænia rhinaris*, PILGER; 1805, *Tænia lanceolata*, RUDOLPHI; 1805, *Cochlus rhinarius*, RUDOLPHI; 1808, *Prionoderma rhinarium*, RUDOLPHI; 1809, *Polystoma tænioides*, RUDOLPHI; 1816, *Linguatula tænioides*, LAMARCK; 1817, *Prionoderma lanceolata*, CUVIER; 1819, *Pentastoma tænioides*, RUDOLPHI; 1828, *Linguatula lanceolata*, DE BLAINVILLE; 1885, *Linguatula rhinaria*, RAILLIET; 1895, *Linguatula caprina*, R. BLANCHARD; 1900, *Linguatula rhinaris*, RAILLIET. Nymphal form; 1789, *Linguatula serrata*, FRÖLICH; 1789, *Tænia caprœa*, ABILDGAARD; 1789, *Tænia caprina*, GMELIN; 1800, *Polystoma serratum*, GOEZE; 1803, *Halysis caprina*, ZEDER; 1805, *Linguatula denticulata*, RUDOLPHI; 1809, *Echinorhynchus capræ*, BRAUN; 1809, *Polystoma denticulatum*, RUDOLPHI; 1810, *Tetragulus caviæ*, BOSC; 1819, *Pentastoma denticulatum*, RUDOLPHI; 1819, *Pentastoma serratum*, RUDOLPHI; 1819, *Pentastoma emarginatum*, RUDOLPHI; 1829, *Pentastoma fera*, CREPLIN; 1840, *Pentastoma tænoides*, DICK (misprint); 1849, *Linguatula ferox*, GROS.

This species has been found in man, both in its nymphal and adult stages. The nymphal form is of frequent occurrence, but is usually overlooked. ZENKER (1854) was the first who noticed its presence in man. He found it in 9 out of 168 postmortems, usually on the liver, invariably encysted and generally calcified. Since then, numerous pathologists have reported its occurrence in man. It appears to have little or no pathogenic importance, and is certainly, in most cases, a harmless pseudo parasite. One positive case only* is known of the presence of the adult form in man. It was described by LAUDON in 1878. The patient harbouring it suffered from epistaxis, almost uninterruptedly for about seven years, until one day, in a fit of sneezing, he ejected from his left nostril a living parasite, which Prof. BENEKE, of Königsberg, stated to be an adult specimen of *Pentastoma tænioides* (=*Linguatula serrata*). The infection was probably contracted in 1870, during the Franco-Prussian war, in which the patient took part. Its first manifestation seems to have been a severe attack of perihepatitis. The liver trouble continued until 1874. The bleeding of the nose began in 1871, soon after the first liver disturbances, and ceased immediately after the expulsion of the parasite. This case is extremely interesting, it appears to suggest that the linguatulid may occasionally go through its entire development within the same host, or at any rate that it may actively migrate from the liver to the nasal cavities after a period of encystment in the liver or other internal organ. Similar cases have been observed

(6) LEUCKART (1860) reports a case described by FULVIUS ANGELINUS in 1610 as possibly pertaining to the adult form of *Linguatula serrata*, but, as already pointed out both by GIARD and BLANCHARD, both the description and figure of the parasite given by ANGELINUS suggest far more likely a myriapod.

in the horse, mule and sheep, herbivorous animals which, as a rule, harbour the nymphal form of the parasite.

*Porocephalus armillatus** is an Ethiopian species widely distributed throughout Tropical Africa. In its adult stage it is a parasite of pythons *(Python saebæ, P. regius)* and puff-adders *(Bitis arietans, B. nasicornis, B. gabonica)*. The nymphal stage has been found in the following mammals: Chimpanzee *(Anthropopithecus troglodytes)*, Sykes's Monkey *(Cercopithecus albigularis)*, Pousargue's Guenon *(C. pousarguei)*, Sooty Mangabey *(Cercocebus fuliginosus)*, Chacma, Baboon *(Papio porcarius)*, Mandrill *(Papio maimon)*, Bosman's Potto *(Perodicticus potto)*, African Hedgehog *(Erinaceus æthiopicus)*, Lion *(Felis leo)*, Leopard *(Felis pardus)*, Kusimanse *(Crossarchus obscurus)*, Banded Ichneumon *(C. fasciatus)*, Aard Wolf *(Protoles cristatus)*, Domestic Dog *(Canis familiaris)*, Black Rat *(Mus rattus)*, Gambian Pouched Rat *(Cricetomys gambianus)*, South African Reedbuck *(Cervicapra arundinum)*, and the Giraffe *(Giraffa camelopardalis)*.

So far, the adult stage of this linguatulid has neither been found in man nor in any other mammal. SHIPLEY

*The synonomy of this species is as follows:—Adult form: 1847. *Linguatula armillata*, WYMAN; 1856, *Pentastomum polyzonum*, HARLEY; 1860, *Pentastomum amillatum*, LEUCKART (misprint); 1863, *Pentastoma armillata*, WYMAN; 1864, *Pentastomum armillatum*, DIESING; 1893, *Porocephalus armillatus*, STILES; 1893, *Porocephalus polyzonus*, STILES; 1899, *Porocephalus moniliformis*, NEUMANN (in part only). Nymphal form: 1849, *Linguatula diesingii*, VAN BENEDEN; 1849, *Pentastomum tornatum*, CREPLIN (in part only); 1850. *Pentastomum euryzonum*, DIESING; 1851, *Nematoideum hominis (viscerum)*, DIESING; 1852, *Pentastomum constrictum*, VON SIEBOLD; 1855, *Linguatula constricta*, KUHENMEISTER; 1863, *Pentastoma leonis*, WEDL; 1864, *Pentastomum leonis*, DIESING; 1879, *Pentastoma tornatum*, COBBOLD; 1883, *Pentastomum protelis*, HOYLE; 1893, *Porocephalus constrictus*, STILES; 1896, *Linguatula constrictor*, GALLI-VALERIO (misprint); 1898, *Pentastomum diesingii*, SHIPLEY.

(1898 and 1908) mentions the lion as a host of the mature form, but this is an error due entirely to oversight. Already 16 cases have been described of the nymphal form in man, but the infection is far more common and widely spread than generally supposed, and its pathogenic importance far greater than that of *Linguatula serrata*. Hitherto the parasite has been found only in African natives, but, given the necessary conditions of infection, it is, of course, quite likely to attack the white man.

*Porocephalus moniliformis** is an Oriental species. It is found in India, Indo-China, Southern China and in the Malay Archipelago. In its adult stage it is a parasite of the Indian Python (*Python molurus*) and the Reticulated Python (*P. reticulatus*). In its nymphal stage it has been found in the following mammals: Macaque Monkey (*Macacus cynomolgus*), Rhesus Monkey (*M. rhesus*), a Sumatran monkey (sp. undetermined), Tiger (*Felis tigris*), Rusty Tiger Cat (*Felis planiceps*), Indian Civet (*Viverricula malaccensis*), Indian Otter (*Lutra nair*).

Twice the nymphal form of this linguatulid has been found in man. The first case was described by Dr. SALM (1906), who found the parasite encysted in the serous coat of the small intestine in a Djambi native, who died of dysentery at Djambi, Sumatra. The second case was reported by HERZOG and HARE (1907), who found the nymphal form in the liver of a native Filipino, who died of tuberculosis in Manila.

*The synonymy of this species is as follows:—Adult form: 1835, *Pentastoma moniliforme*, DIESING; 1860, *Pentastomum moniliforme*, LEUCKART; 1880, *Linguatula moniliforme*, MÉGNIN; 1893, *Porocephalus moniliformis*, STILES. Nymphal form: 1849, *Pentastoma tornatum*, CREPLIN (in part only); 1866, *Pentastoma wallii*, COBBOLD; 1874, *Pentastoma aonyeis*, MACALISTER; 1908, *Porocephalus armillatus*, STILES (in part only).

Porocephalus armillatus and *P. moniliformis* have often been confounded. MÉGNIN (1880), under the name of "Pentastome moniliforme," confounds a number of distinct species (*Porocephalus crotali*, *P. clavatus P. armillatus*, *P. moniliformis*, *Reighardia oxycephala*, etc.), as may be inferred from the names of the animals mentioned as hosts (rattle-snakes, boas, crocodiles, monitors, etc.), and from the drawings given as representations of the species in its various stages. NEUMANN (1899) wrongly ascribes to the species *P. moniliformis* certain nymphal linguatulids found in the mesentery of young dogs reared in his laboratory, where, a few weeks before their birth, he had dissected two specimens of *Python natalensis* (*P. Sebæ*) in the lungs and tracheæ of which he found numerous specimens of a linguatulid, he mistook for *P. moniliformis*. NEUMANN was probably led into error by MÉGNIN, who had previously erroneously ascribed to the Oriental species the tongue-worms found by BOCHEFONTAINE in another laboratory dog similarly infected. At the same time, it is necessary to point out that several authors have confounded not only *P. moniliformis* with *P. armillatus*, but also the Indian pythons with the African pythons. LOOSS (1905) in MENSE'S "Handbuch der Tropenkrankheiten," ascribes the nymphal tongue-worm found in man in Africa to *P. moniliformis*, stating, however, that he considers this species identical with *P. armillatus*. He says, "The adult animal is without doubt *Porocephalus moniliformis*, DIESING," and he gives two drawings of the adult form which he states are from the lungs of *Python sebæ*, but the largest specimen shows 30 distinct rings, and the smaller one over 26. It is obvious, therefore, that the specimens delineated could not have been found in a West African

python under natural conditions, and do not represent the African tongue-worm, but are certainly of Oriental origin. Finally, STILES (1907), in his very valuable paper, "The Zoo-parasitic Diseases of Man," contributed to "A System of Medicine," edited by Professors OSLER and MCCREE, says "*Porocephalus moniliformis*, DIESING (1836) is an African Tongue-worm," and in a later publication erroneously ascribes to *Porocephalus constrictus* (= *P. armillatus*) the linguatulid found by HERZOG and HARE in a native Filipino in Manila.

As I have already pointed out, on various occasions, *P. armillatus* and *P. moniliformis* are two distinct species. *P. armillatus* is limited to the Ethiopian region, comprising Africa, south of the Atlas, and Arabia. It is characterised by the presence of 16 to 17 rings in the male, 18 to 22 in the female. *P. moniliformis* presents 26 rings in the male, 29 to 33 in the female. The body tapers decidedly more in the Oriental species, and the annulations are less prominent and more bead-like than in the African species.

In addition to the three species just mentioned, it is very probable that other species occur in man. I have little doubt that, with a more extended knowledge of the zoo-parasitic diseases of Tropical America, we shall have to enumerate *Porocephalus crotali*, *P. clavatus*, *P. stilesi* and other Neotropical species amongst the linguatulids which may occasionally occur in man during their nymphal stage. Indeed, some cases have already been reported from America, as, for instance, those published by FLINT, OSLER and SANCHES.

Dr. FLINT'S case is of considerable interest. The patient, a farmer of Albany, Gentry Co., Mo., was 36 years of age; he had served three years in the army

during the war. When examined by his physician, Dr. M. M. CAMPBELL, he was found to be greatly emaciated, and of sallow complexion; his liver was greatly enlarged and very tender on pressure, his left lung presented two cavities and for about a month he had been coughing up or vomiting a large number (75 to 100) of parasites which crawled about the floor like maggots. One of the parasites together with the history of the case were sent to Dr. FLINT, who, having read AITKEN'S account of a similar case in a negro soldier, who died in Jamaica about eight months after enlistment from the slave depôt in St. Helena, considered the parasites to be specimens of *Pentastoma constrictum (= Porocephalus armillatus)*. It is obvious, however, that FLINT'S determination is erroneous, because if the parasite in CAMPBELL'S case was really an immature linguatulid, as seems probable, it could not have been the African one, but some indigenous species, possibly *Porocephalus crotali*, a tongue-worm of the Diamond Rattle Snake *(Crotalus adamanteus)*, which inhabits the Southern United States.

Prof. OSLER'S case is very briefly stated. Writing of *Porocephalus constrictus*, at p. 375 of his "Principles and Practice of Medicine," he says: "In 1869 I saw a specimen which had been passed with the urine by a patient of JAMES H. RICHARDSON, of Toronto." The escape of the parasite by way of the urethra would suggest a Sparganum, but Prof. OSLER tells me that the specimen was determined by Prof. HINCKS, the zoologist, as *P. constrictum*. It may have been a specimen of *Porocephalus crotali*,

Of SANCHEZ' cases I have the mere reference which mentions the finding of *Pentastoma tænioides (Linguatula serrata)* and *Pentastomum constrictum (Porocephalus*

armillatus) in the stomach and liver respectively of Man in Mexico. Here again *P. armillatus* is very unlikely to be the species found.

In the *Lancet* of November 16th, 1872, is a paper by WELCH, entitled, "The presence of an encysted Echinorhynchus in Man," in which the author describes a minute zoo-parasite found encapsuled in the submucous tissue of the jejunum of a soldier, who had been invalided from Kussowlie for tuberculosis after 16 years' service, the last 14 of which had been spent continuously in India. The parasite consisted of a cylindrical body, measuring a 13th of an inch in length and 033 in thickness; the maximum width was at about the centre of the body, the narrowest part preceding the posterior end, which was bulbous: the anterior end was also rounded and larger than the other, but somewhat flattened. Over the surface of the anterior end were irregularly dispersed a number of hooklets. Immediately below the region of the hooklets there was a slight neck-like constriction. Over the body generally there were numerous irregular lines showing a wrinkling of the outer surface. The hooklets were of two forms, one had a broad base attachment, and springing from it a very sharply curved claw: the other with a narrower base, presented a long straight limb rising almost at right angles from it, and a sudden curved sharp tip. They were hollow, of a bright amber colour, and contrasted strongly with the dull opalescent aspect of the body generally. The author states that the hooklets were either seen in their entirety or merely the disc of attachment, and that not more than nine could be counted. Considering that further he states that the animal had no mouth and that it was examined under

considerable pressure, we can safely surmise that the mouth was taken for one of the discs of attachment, that the hooklets were eight in number, and that, owing to manipulation, they had been broken and displaced.

Cobbold (1879) pointed out that Welch's parasite was not an Echinorhynchus, but a linguatulid, and stated that "If it be not the *Pentastoma denticulatum (=Linguatula serrata)*, it must either be referred to *P. constrictum* (in an early larval condition), or to some other hitherto undescribed pentastomatoid larva." Prof. Blanchard (1890) also considered Welch's parasite to be a linguatulid, but not *Linguatula serrata*. Judging from the region in which the infection took place, the size of the parasite, the cylindrical form of its body, the number and shape of its hooklets, I should be inclined to suggest, though very reservedly, that Welch's linguatulid might possibly have been a specimen of *Porocephalus najæ*, a parasite found by Leuckart (1860) encysted amongst the abdominal muscles and on the peritoneum of the Indian Cobra *(Naja tripudians)*, or again, unless the two be identical, the one found by Parona (1890) in Blyth's Musk-Shrew *(Crocidura fuliginosa)* and termed by him *Pentastomum crociduræ*.

From what I have said, you will have gathered that these vermiform, endoparasitic arthropods play a non-unimportant part in human pathology, and that they are well worth our consideration. Few animals are of greater interest; believed at first to be Cestodes, Acanthocephala, Trematodes or Nematodes, later classed among Crustaceans and Arachnida, their systematic positions is still unsettled. With Schubart and Leuckart, I consider that they belong to the order Acarina. Like the ectoparasitic ticks, they are blood suckers

and seem to be concerned in the sporogonic cycle of the hæmogregarines peculiar to their reptilian hosts. PROWAZEK (1908) was the first to point out that the Linguatulidæ probably play a part in the transmission of blood protozoa. He is stated to have found free and encysted oökinetes of *Hæmogregarina pythonis* in the stomach of four specimens of *Porocephalus moniliformis* from a Javanese python *(P. reticulatus)*. Immediately after reading PROWAZEK'S paper, I examined some specimens of *Porocephalus stilesi* taken from the lung of a Curucucu *(Lachesis mutus)*, the blood of which presented numerous sporonts of a new hæmogregarine I have named *Hæmogregarina seligmanni*, with the result that I also found the sporogonic forms of this hæmoprotozoon in the American tongue-worm. LAVERAN (1909) has also confirmed PROWAZEK'S discovery. Already, in 1905, Capt. PATTON had seen in *Porocephalus pattoni* cysts containing Sporoblasts full of Sporozoites, but he did not recognise their true nature, and, indeed, in a recent paper (1909) says: "I now know these cysts represent part of the cycle of a parasite peculiar to the Pentastome, and have nothing to do with the hæmogregarine of the snake." Relying on my own observations, I cannot agree with Capt. PATTON'S opinion, and believe that the cysts observed by PROWAZEK, LAVERAN, PATTON and myself, in various species of tongue-worms do belong to the sporogonic cycle of the hæmogregarines peculiar to their respective hosts.

In connection with the rôle played by the Linguatulidæ in the life-history of the hæmogregarines, it is interesting to recall that JACOB, of Forlì, a Paduan professor of the fourteenth century, in his commentaries on Avicenna, discussing a passage in which the Arab physician says

that worms in the head are very rarely found beneath the meninges, but frequently in the nasal fossæ, states that rabies in the dog is believed to arise from a worm born in its brain. Now, we know that rabies is due to a protozoal organism discovered by NEGRI, and although the disease is only too easily transmitted by the bite of rabid animals, the agency of an animate carrier playing the part of definitive host in the life history of the parasite is not only not excluded, but even probable. In certain forms of trypanosomiasis (Dourine, Sleeping Sickness), and in other protozoal infections (Relapsing Fever, Yaws), we can find the support of analogy for the idea of linking the causative agent of hydrophobia with *Linguatula serrata*.

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